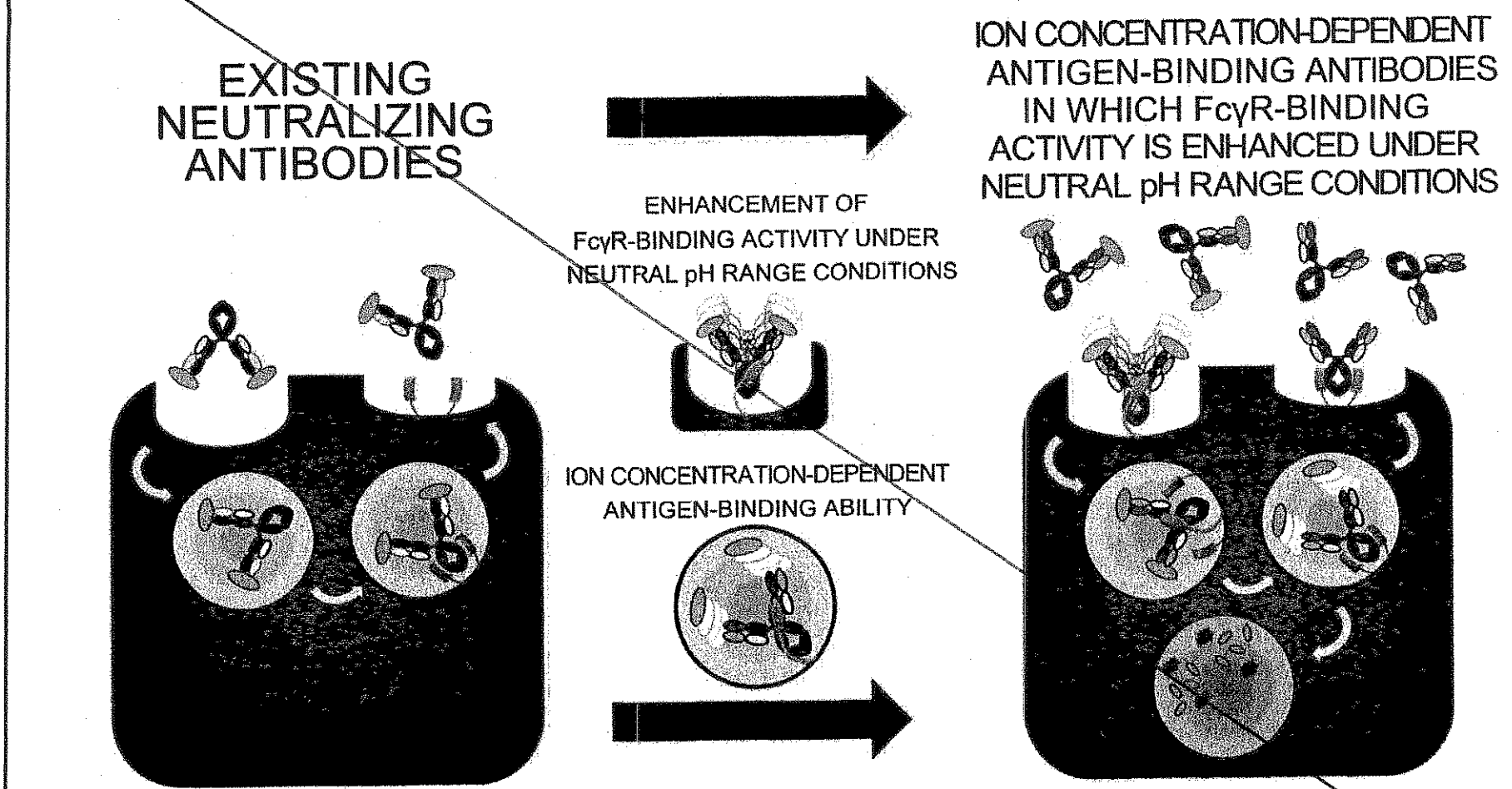

EXISTING NEUTRALIZING ANTIBODIES
ENHANCEMENT OF FcγR-BINDING ACTIVITY UNDER NEUTRAL pH RANGE CONDITIONS
ION CONCENTRATION-DEPENDENT ANTIGEN-BINDING ABILITY
ION CONCENTRATION-DEPENDENT ANTIGEN-BINDING ANTIBODIES IN WHICH FcγR-BINDING ACTIVITY IS ENHANCED UNDER NEUTRAL pH RANGE CONDITIONS

FIG. 1

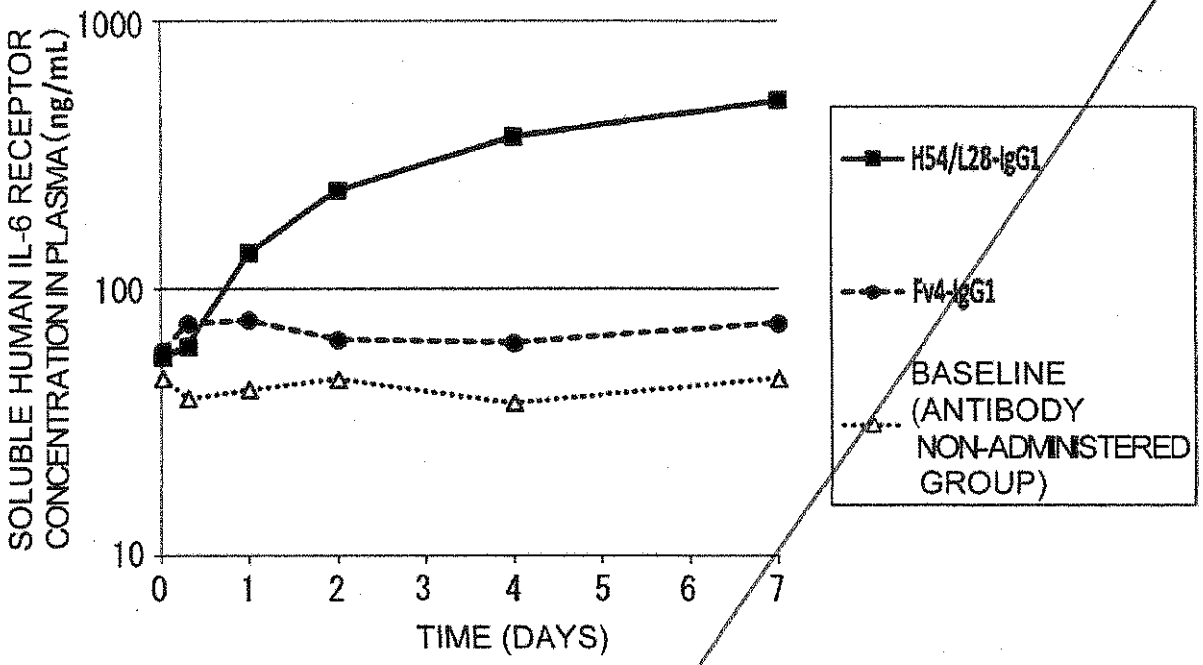

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
0
1
2
3
4
5
6
7
TIME (DAYS)
H54/L28-IgG1
Fv4-IgG1
BASELINE (ANTIBODY NON-ADMINISTERED GROUP)

FIG. 2

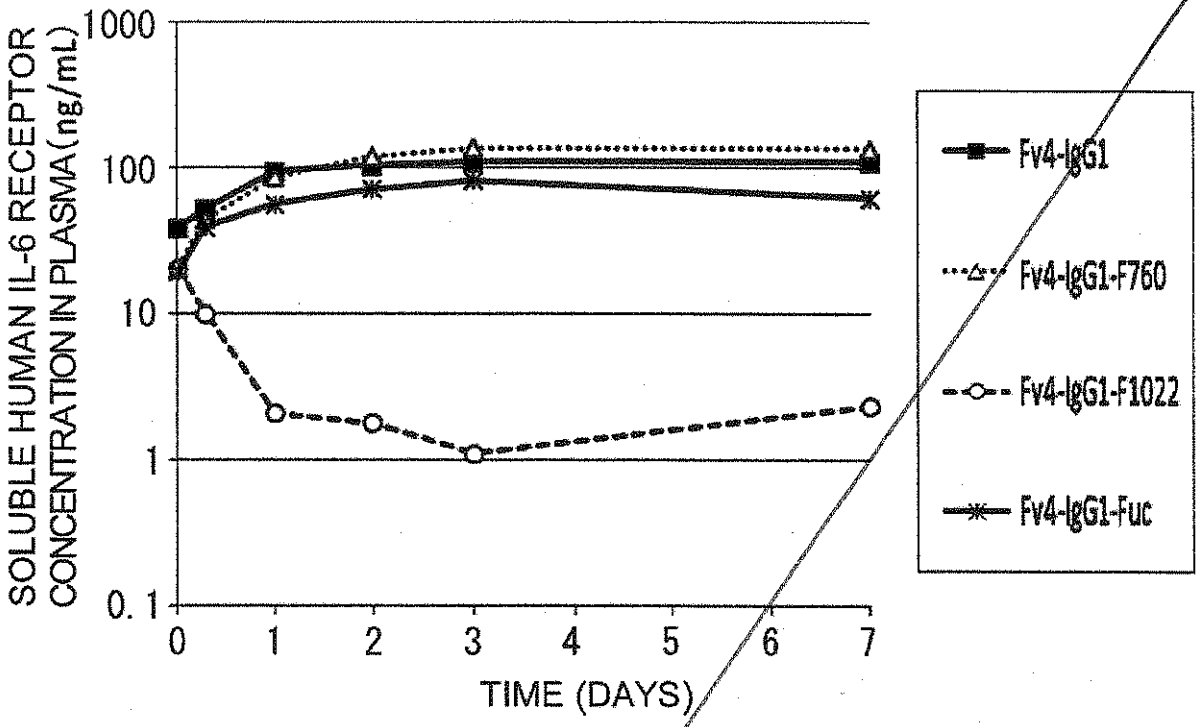

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F760
Fv4-IgG1-F1022
Fv4-IgG1-Fuc

FIG. 3

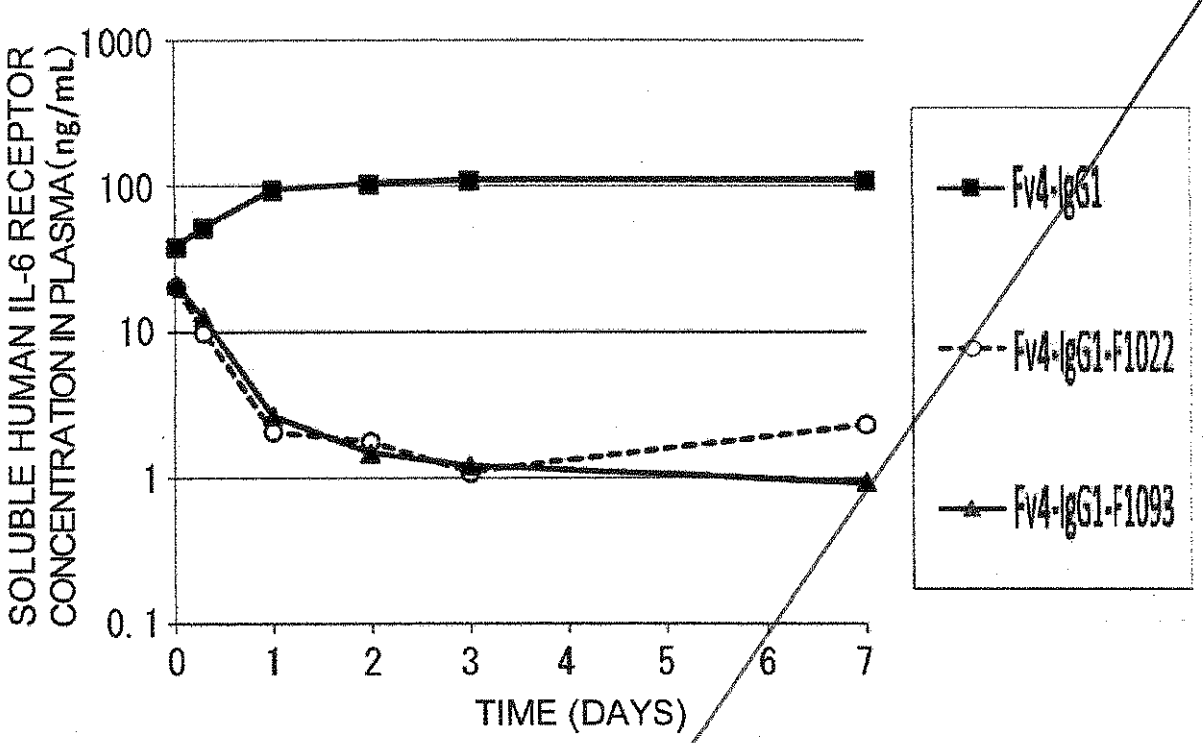

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1022
Fv4-IgG1-F1093

FIG. 4

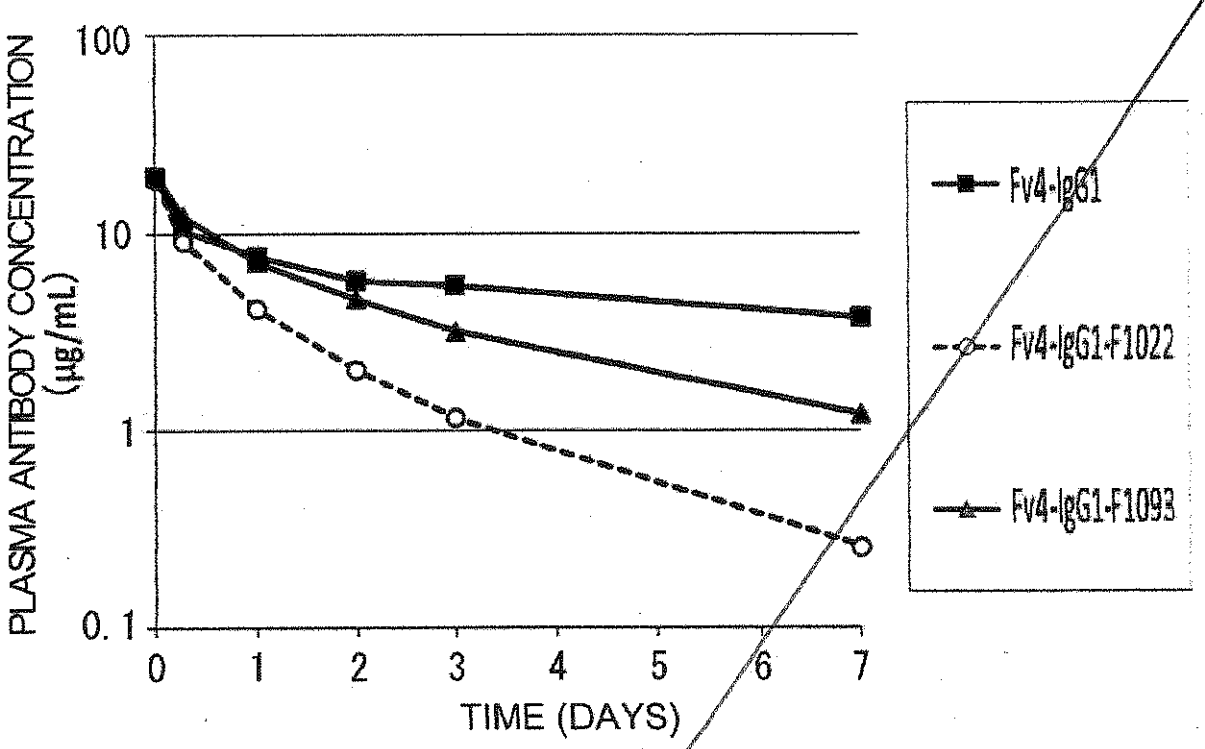

PLASMA ANTIBODY CONCENTRATION (μg/mL)
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1022
Fv4-IgG1-F1093

FIG. 5

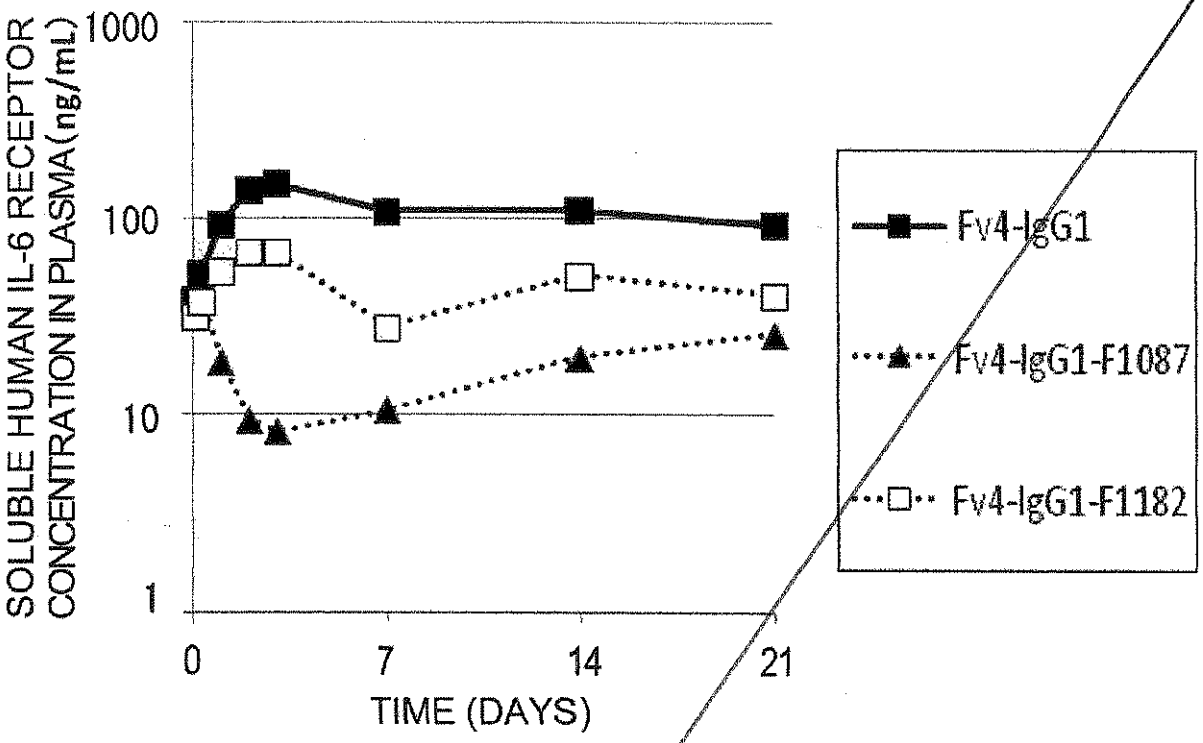

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1182

FIG. 6

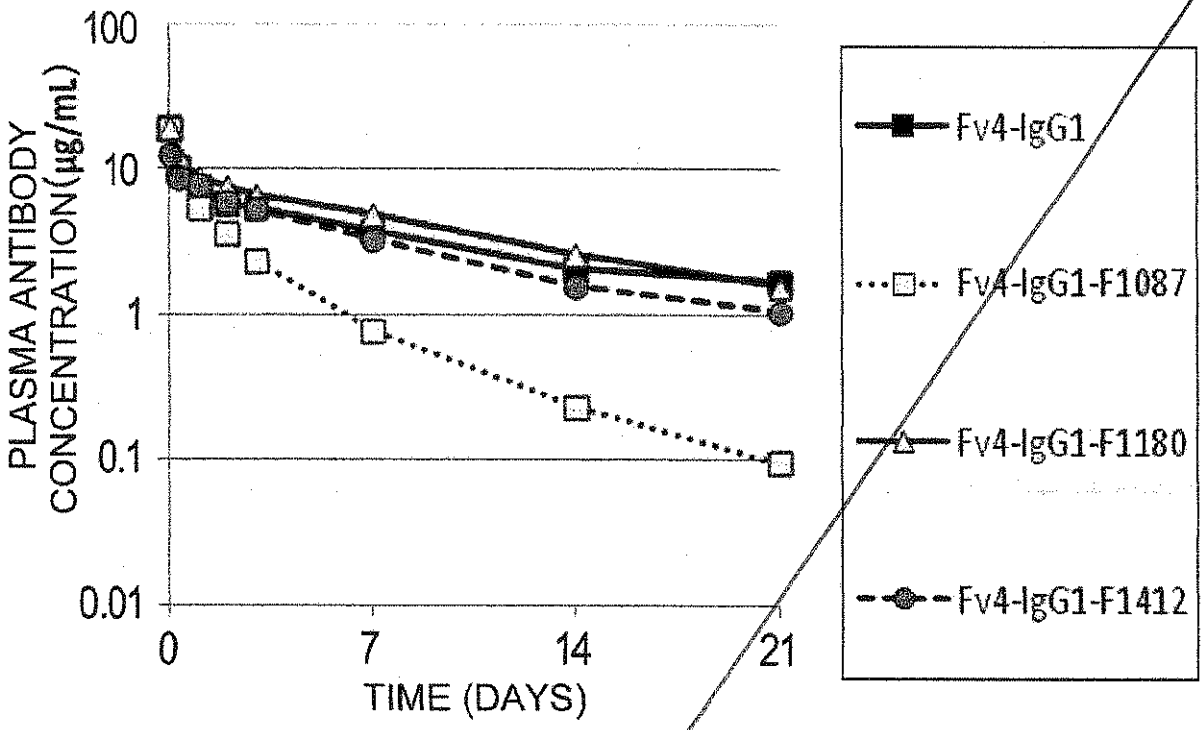

100
10
1
0.1
0.01
PLASMA ANTIBODY CONCENTRATION(µg/mL)
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1180
Fv4-IgG1-F1412

FIG. 7

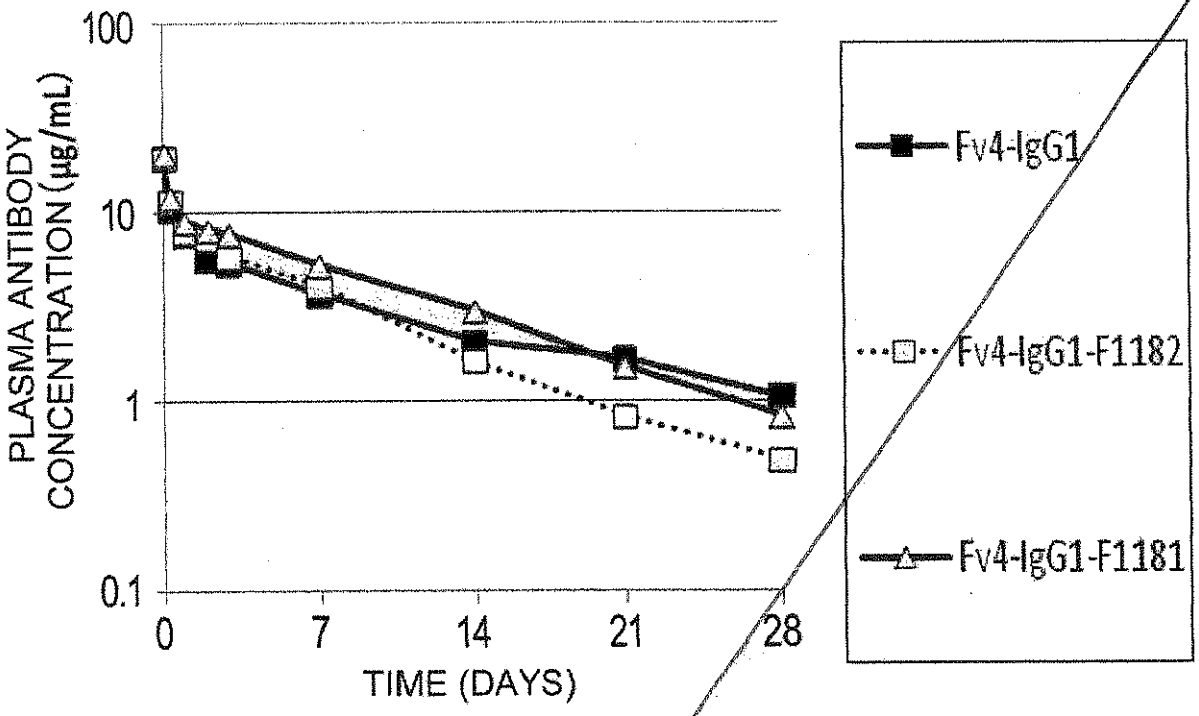

100
10
1
0.1
PLASMA ANTIBODY CONCENTRATION (µg/mL)
0
7
14
21
28
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1182
Fv4-IgG1-F1181

FIG. 8

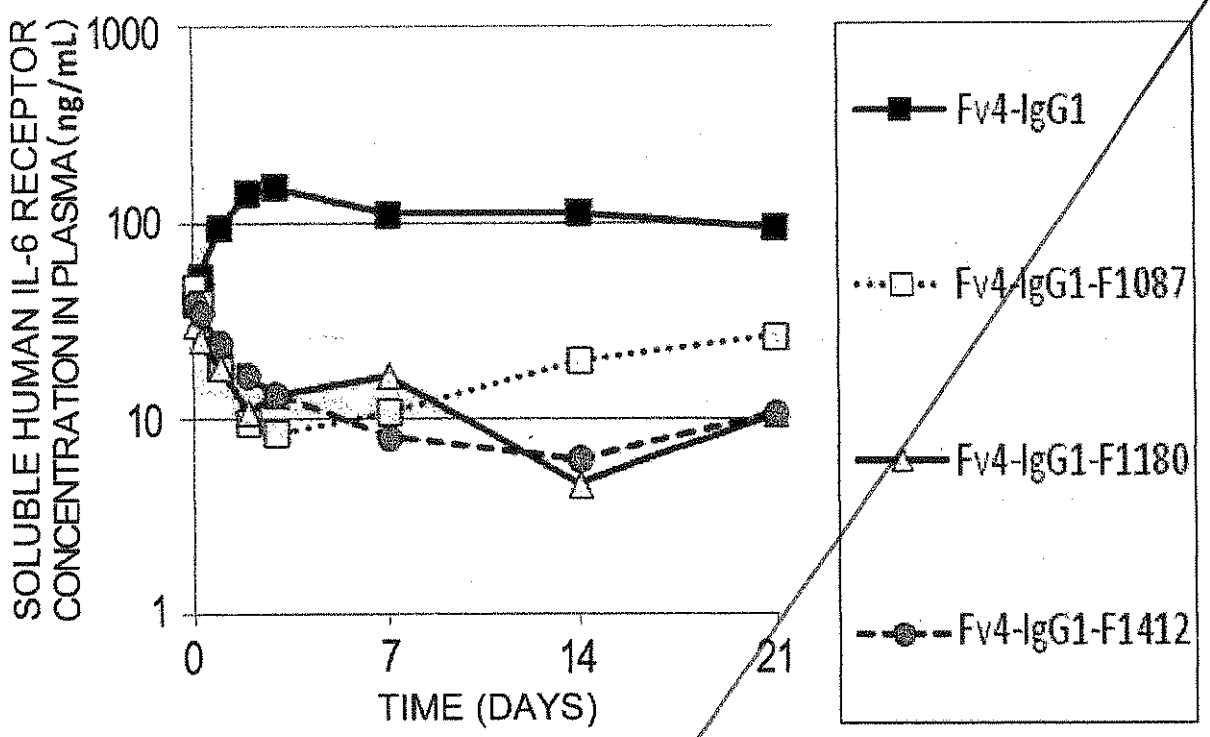

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1180
Fv4-IgG1-F1412

FIG. 9

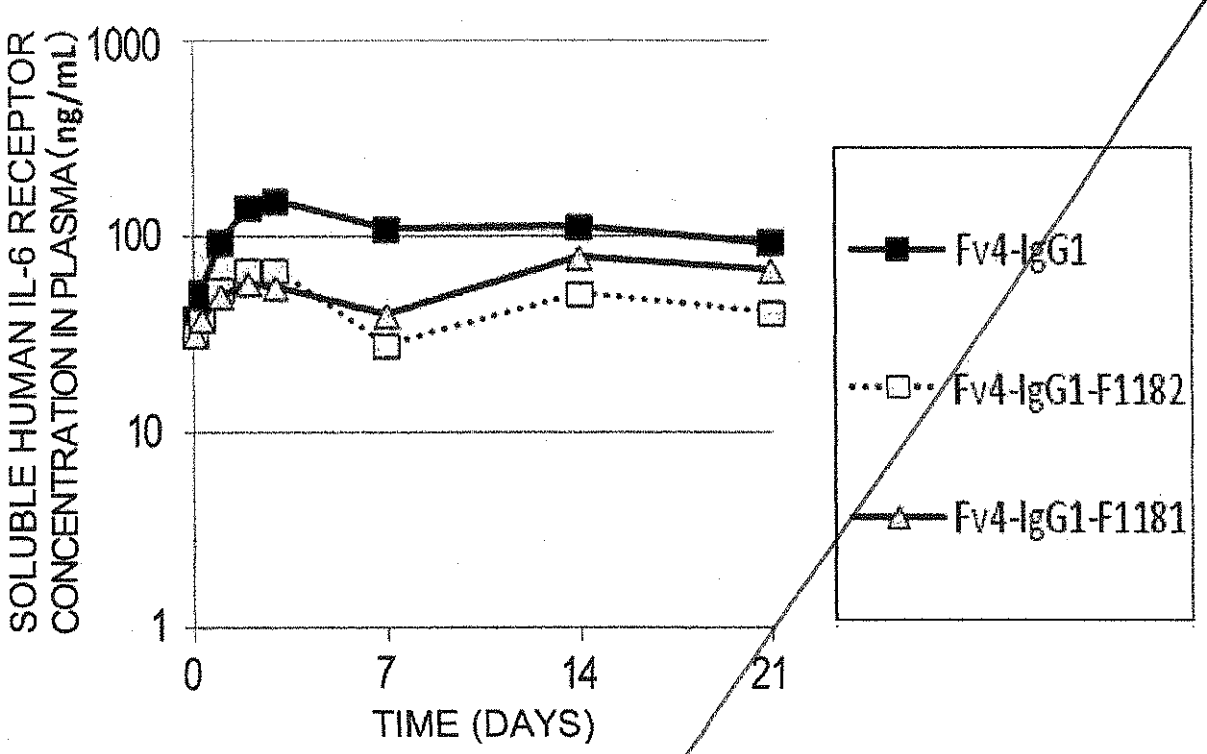

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1182
Fv4-IgG1-F1181

FIG. 10

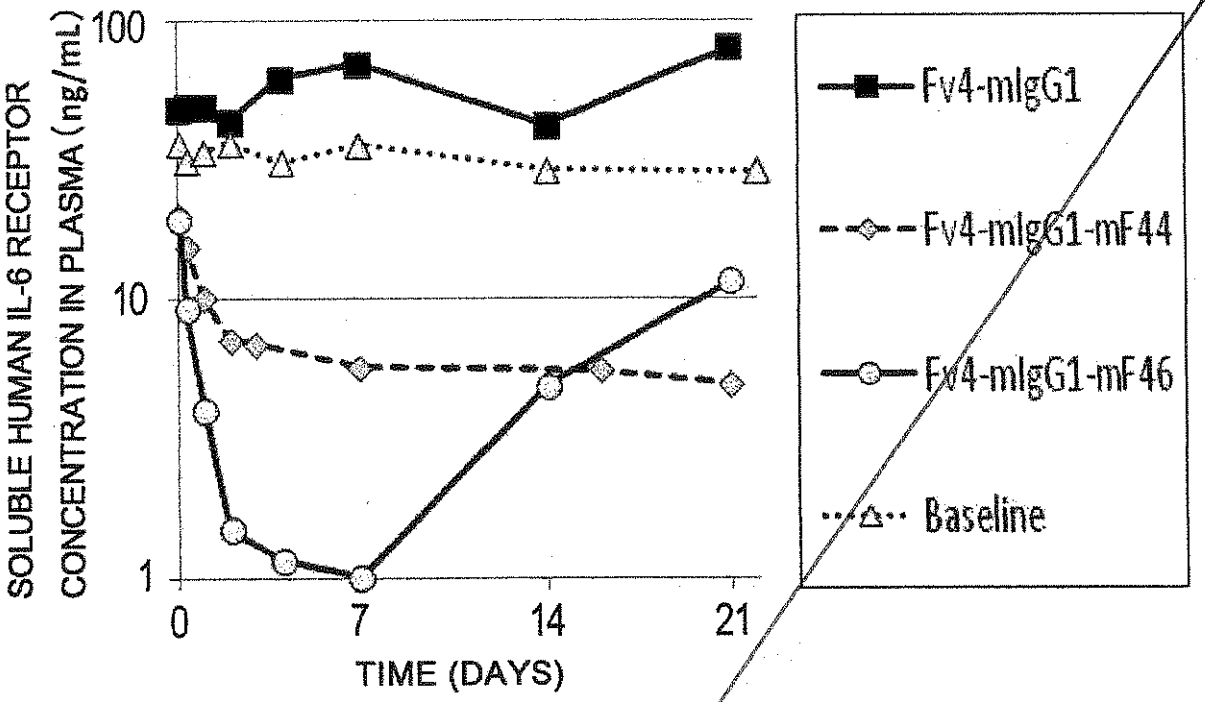

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
Baseline

FIG. 11

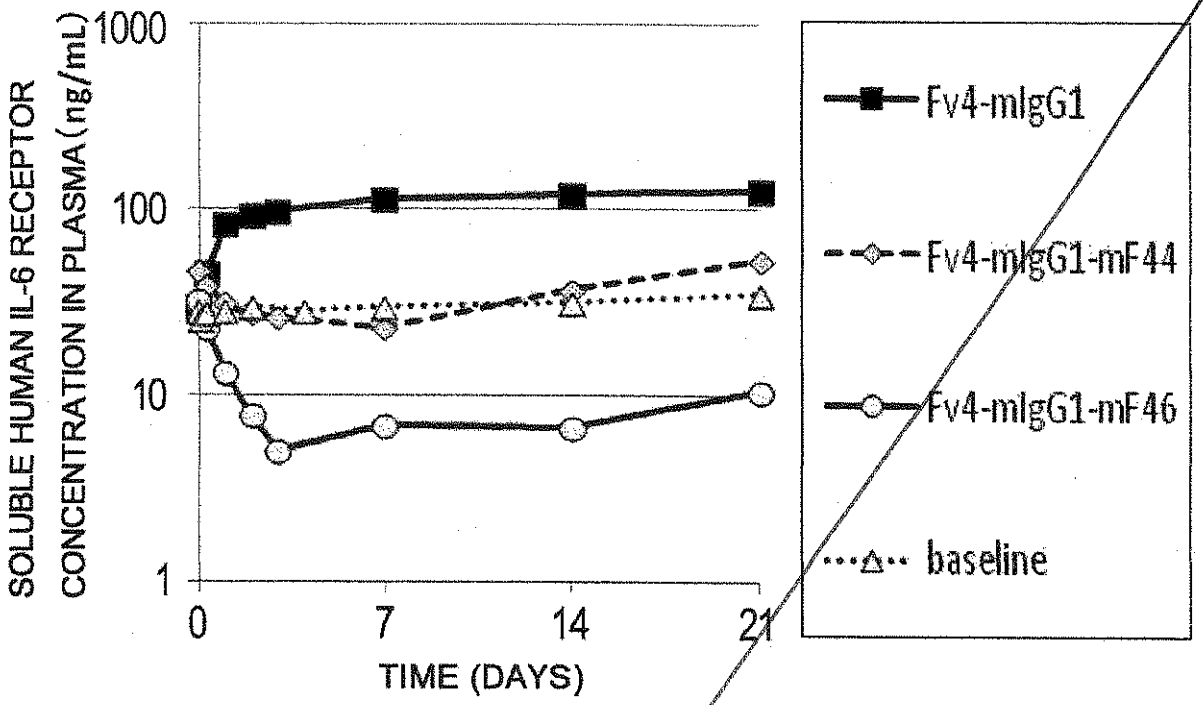

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 12

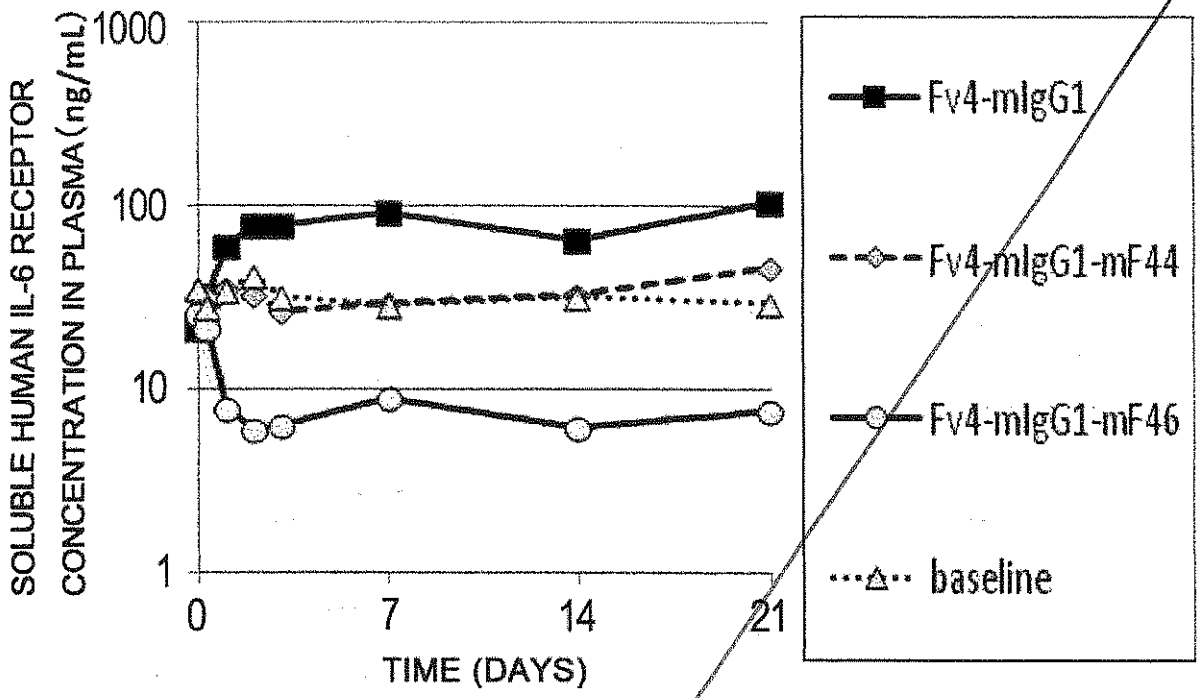

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 13

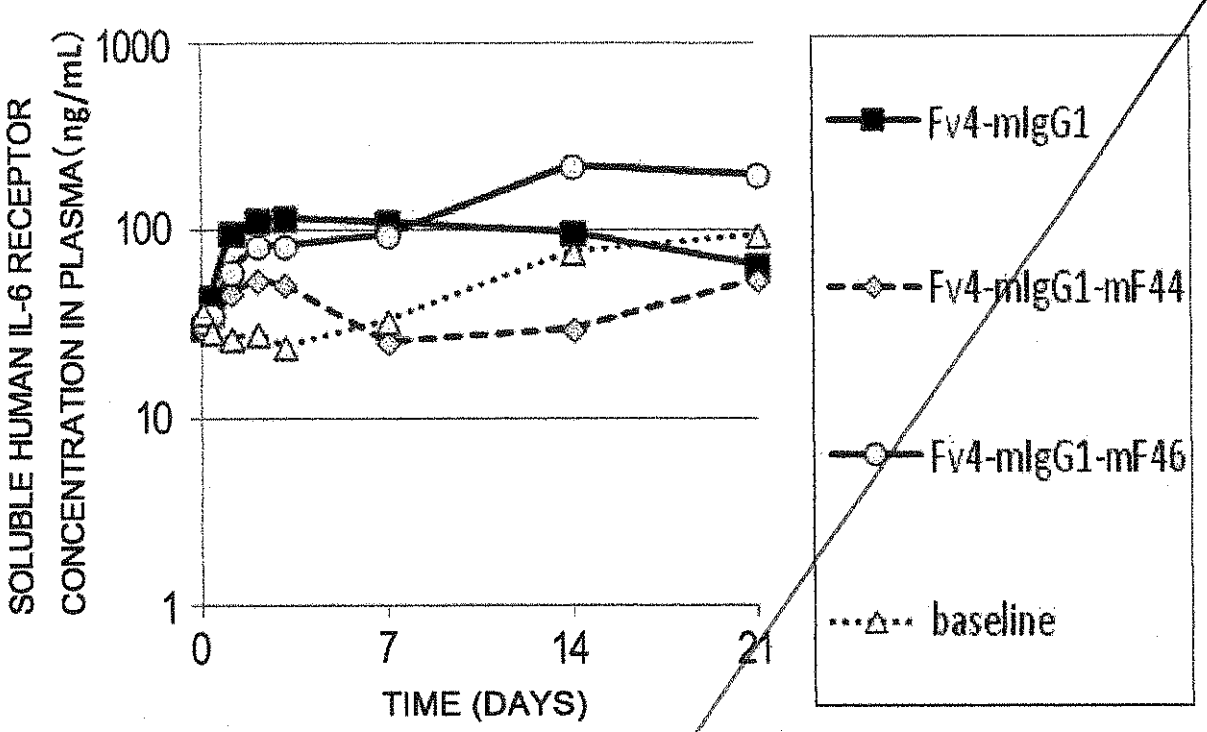

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 14

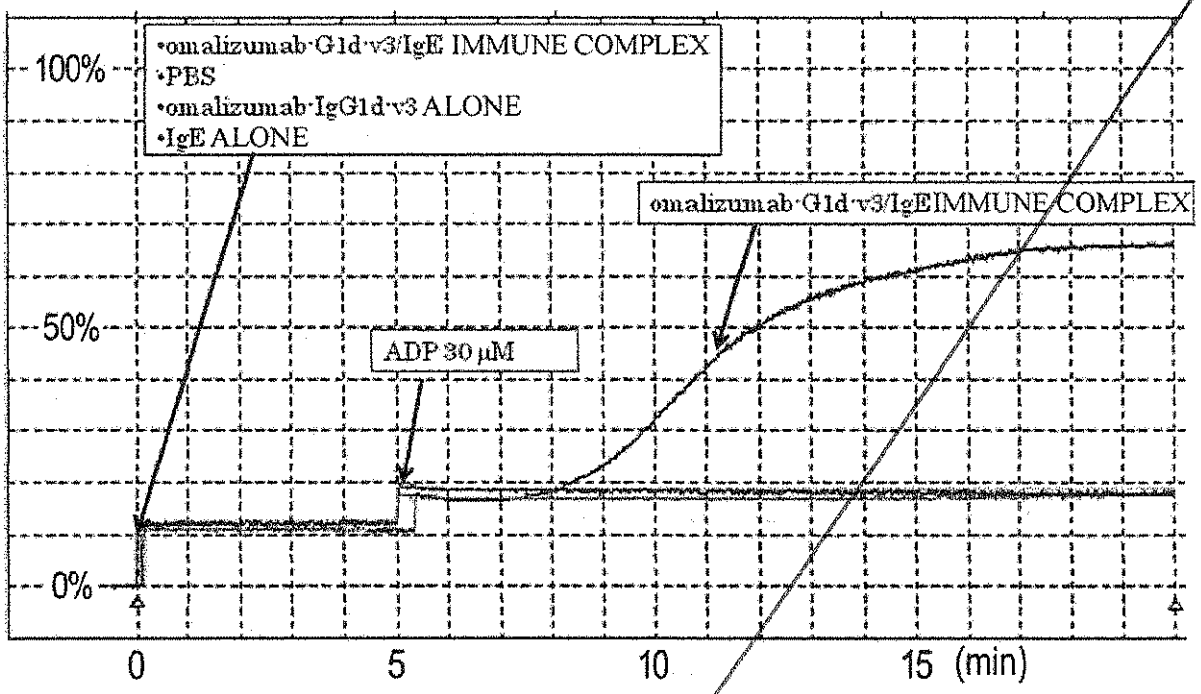

•omalizumab-G1d-v3/IgE IMMUNE COMPLEX
•PBS
•omalizumab-IgG1d-v3 ALONE
•IgE ALONE
100%
50%
0%
ADP 30 μM
omalizumab-G1d-v3/IgE IMMUNE COMPLEX
0
5
10
15 (min)

FIG. 15

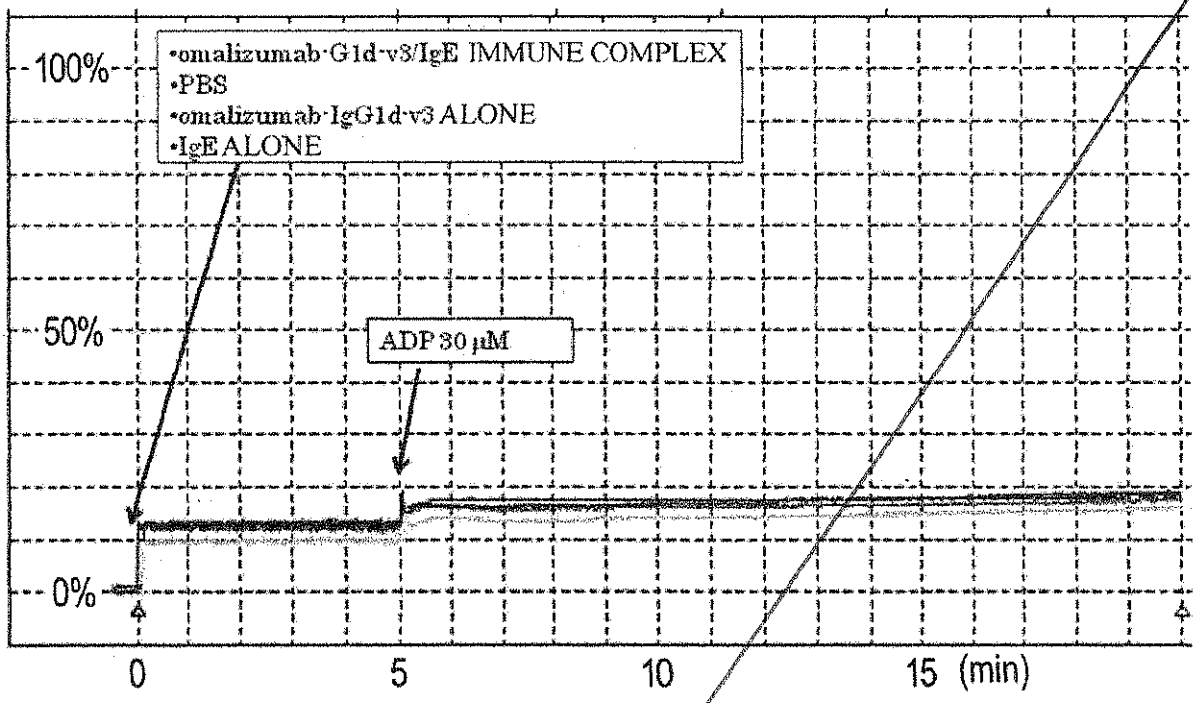

•omalizumab·G1d·v3/IgE IMMUNE COMPLEX
•PBS
•omalizumab·IgG1d·v3 ALONE
•IgE ALONE
100%
50%
0%
ADP 30 μM
0
5
10
15 (min)

FIG. 16

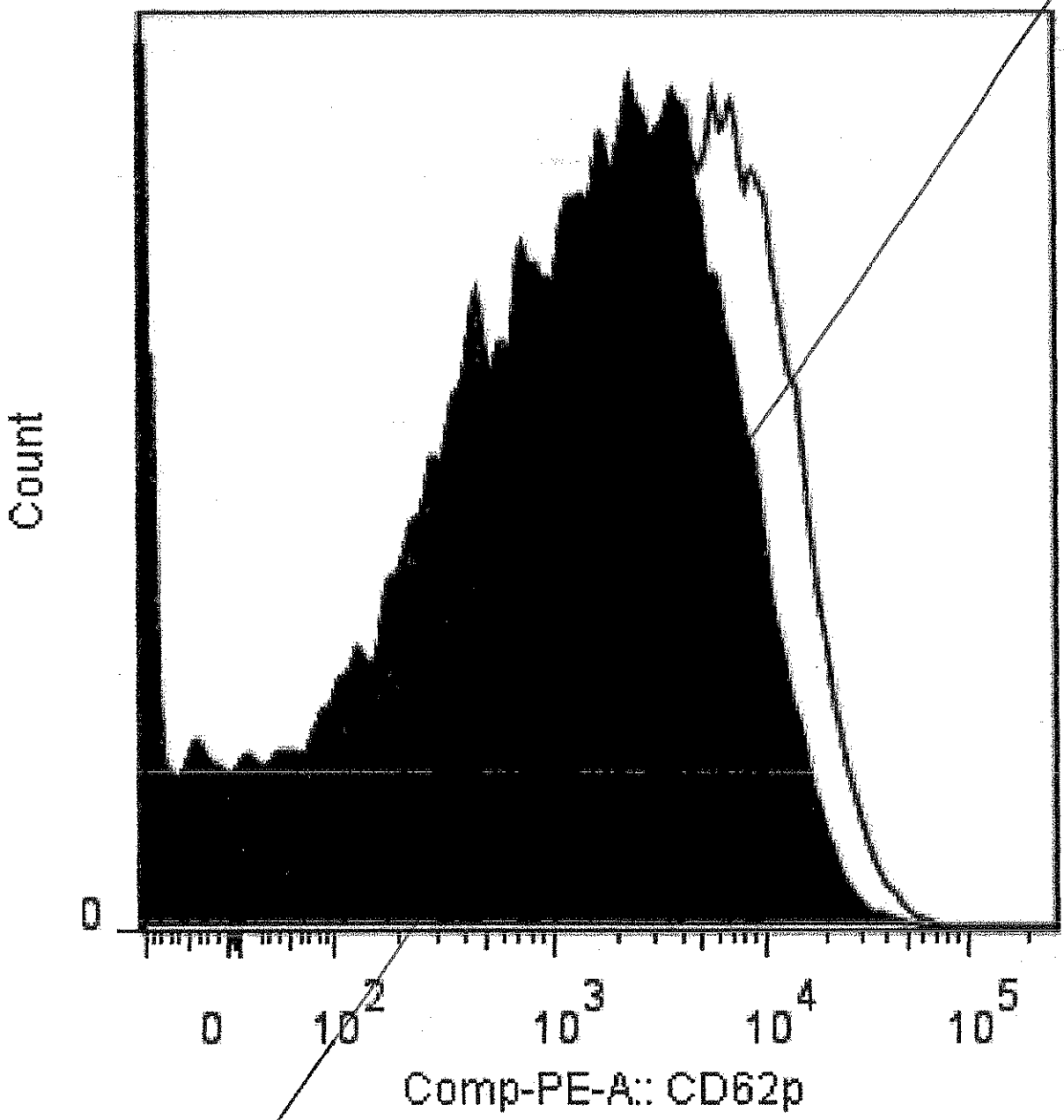


FIG. 17

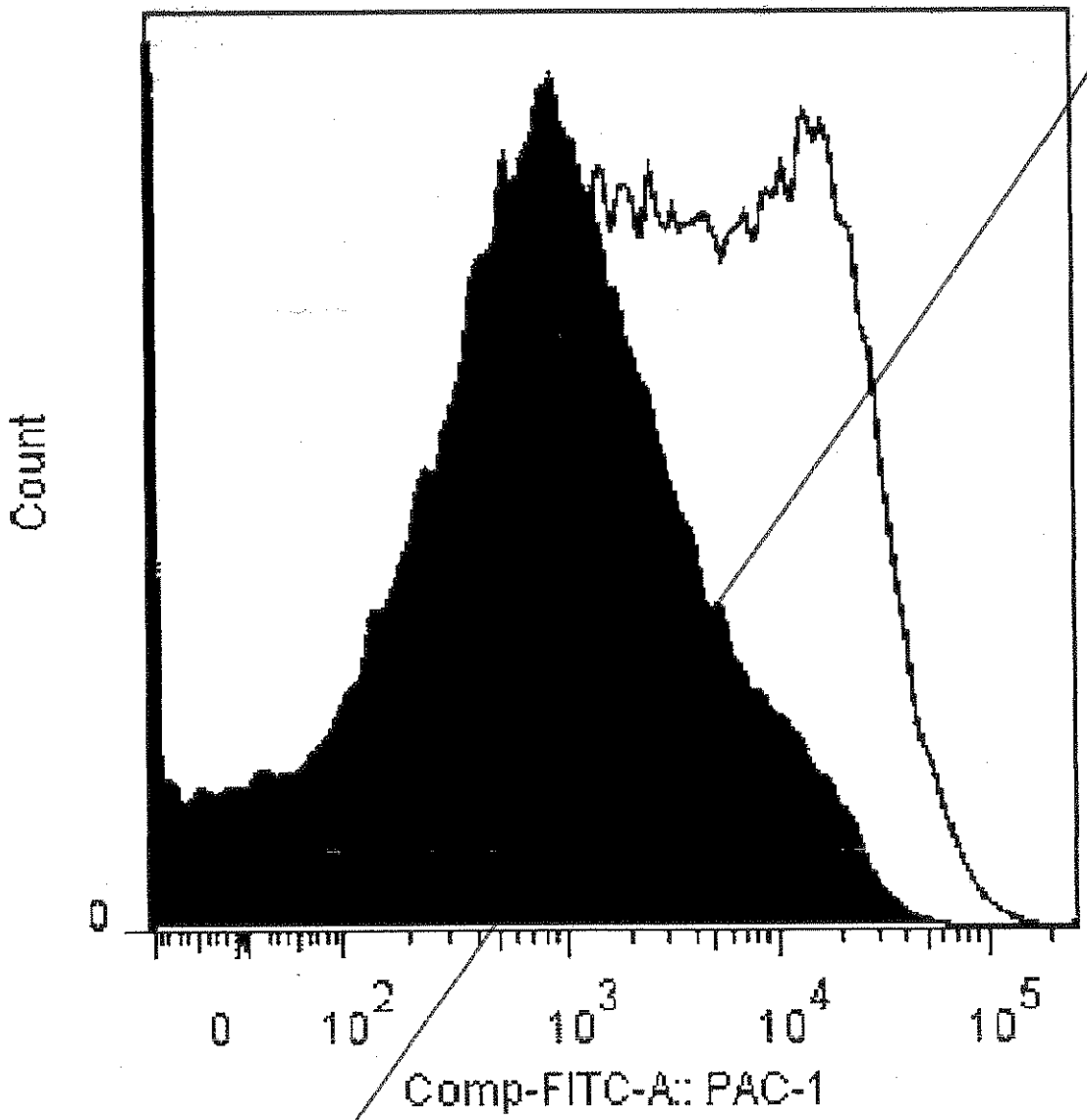


FIG. 18

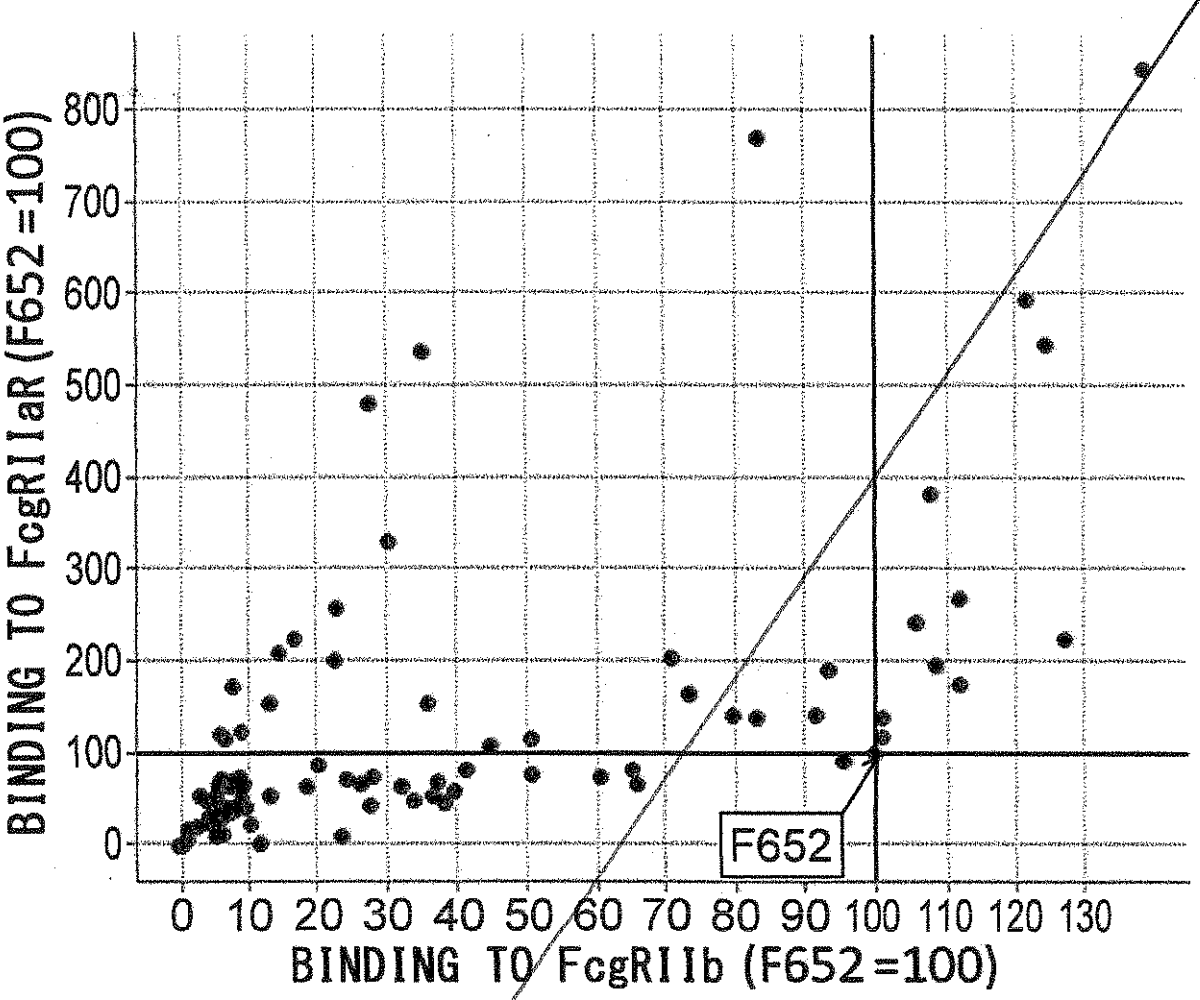

BINDING TO FcgRIIaR (F652=100)
800
700
600
500
400
300
200
100
0
F652
0 10 20 30 40 50 60 70 80 90 100 110 120 130
BINDING TO FcgRIIb (F652=100)

FIG. 19

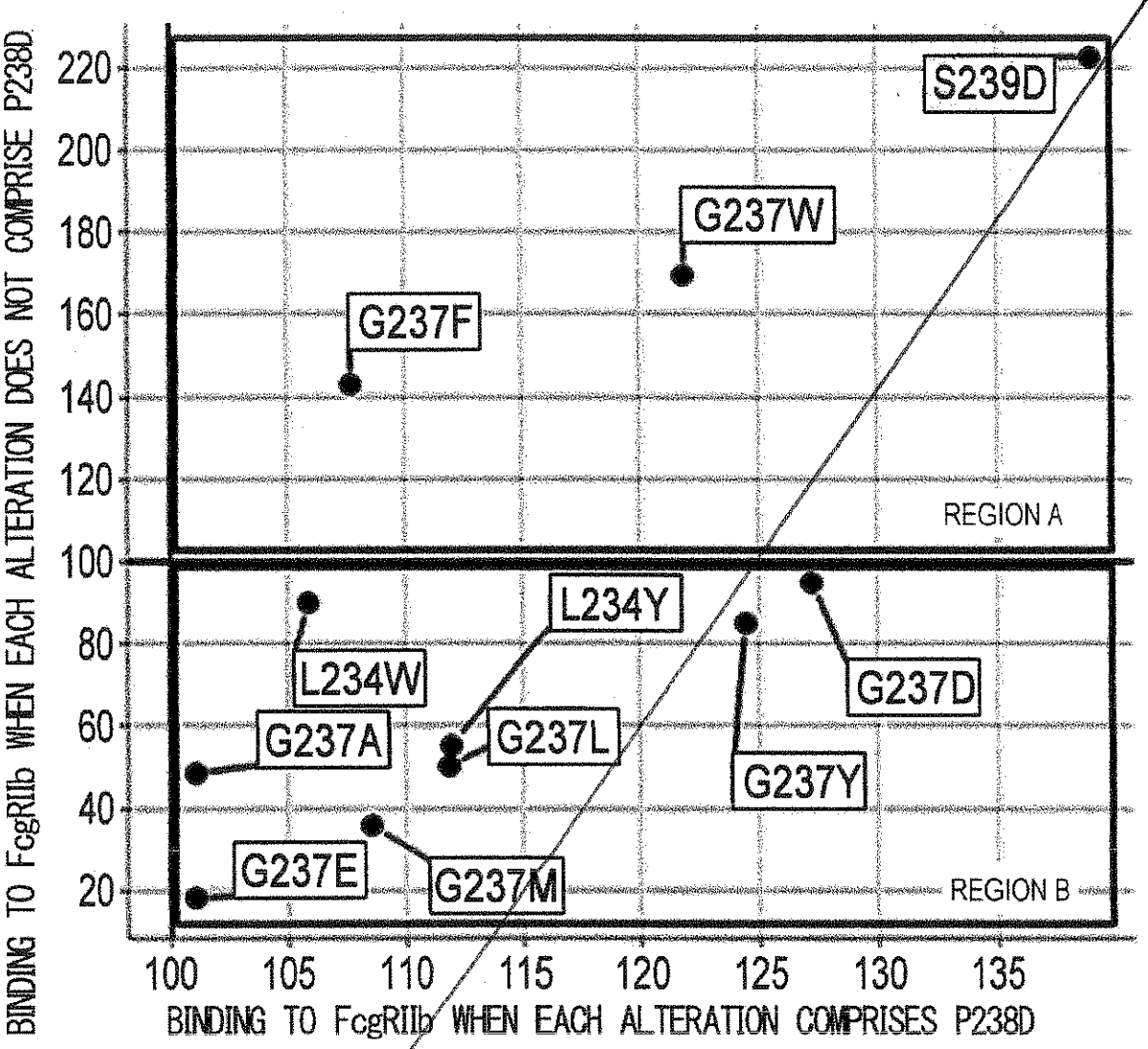

BINDING TO FcgRIIb WHEN EACH ALTERATION DOES NOT COMPRISE P238D
220
200
180
160
140
120
100
80
60
40
20
100
105
110
115
120
125
130
135
BINDING TO FcgRIIb WHEN EACH ALTERATION COMPRISES P238D
S239D
G237W
G237F
REGION A
L234Y
L234W
G237D
G237A
G237L
G237Y
G237E
G237M
REGION B

FIG. 20

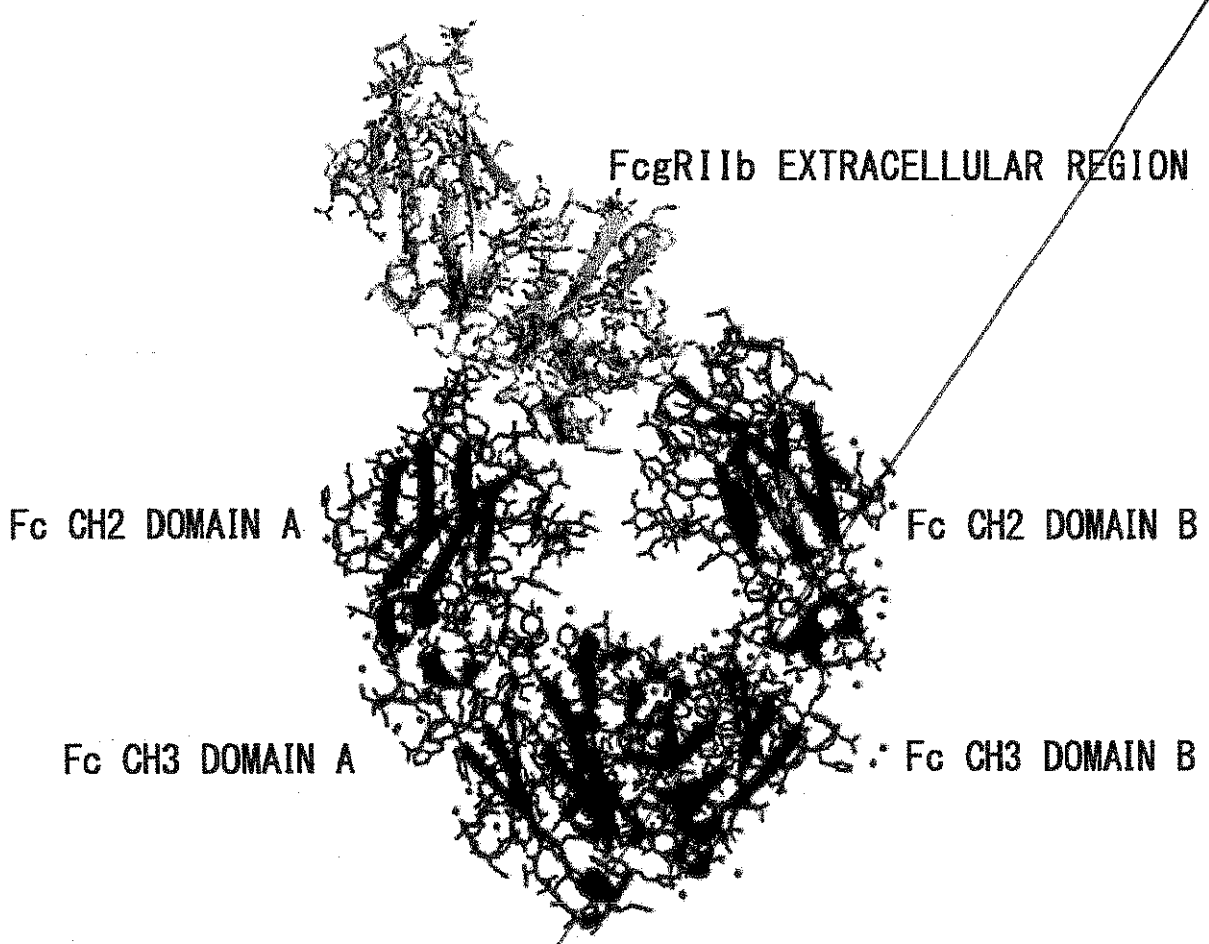
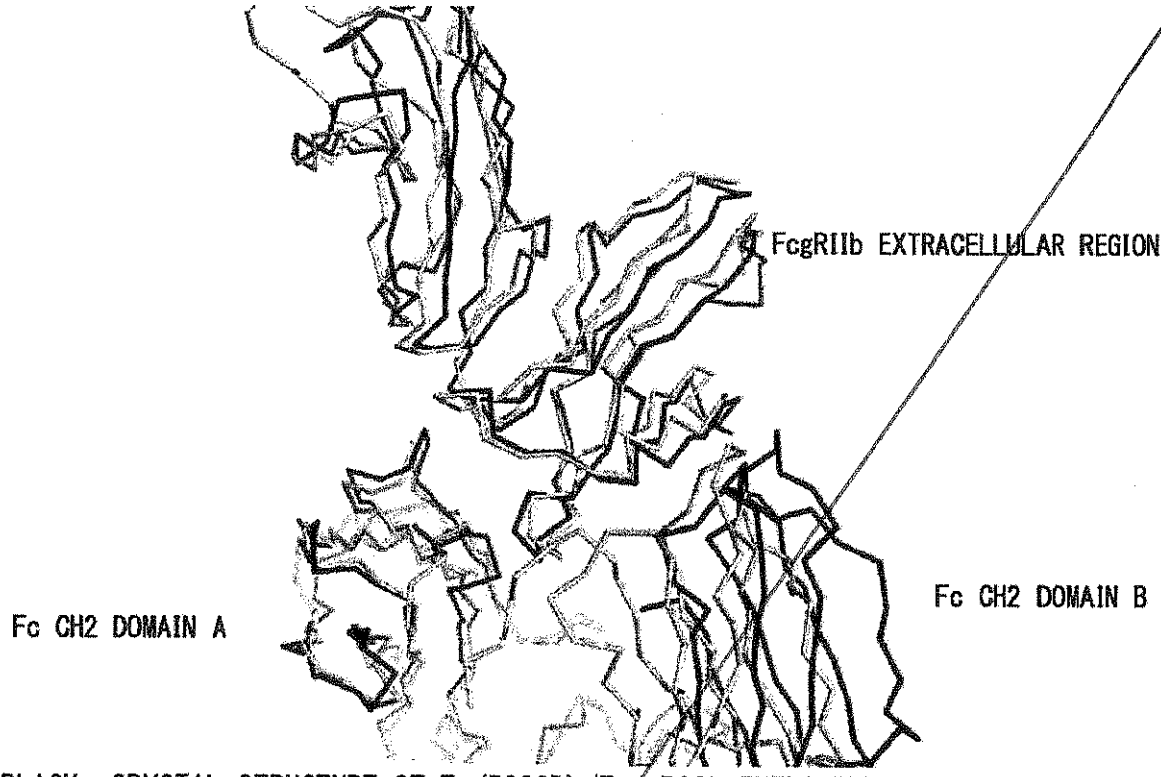
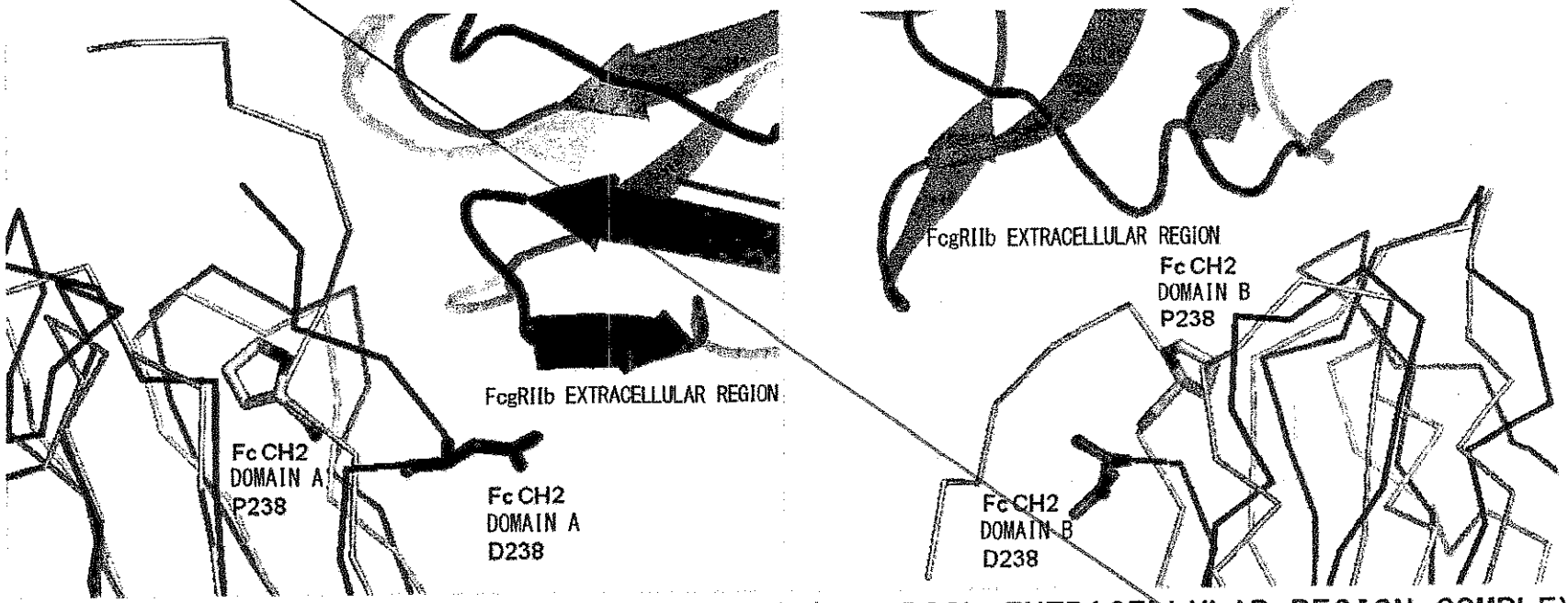

FcgRIIb EXTRACELLULAR REGION
Fc CH2 DOMAIN A
Fc CH2 DOMAIN B
Fc CH3 DOMAIN A
Fc CH3 DOMAIN B

FIG. 21



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX
GRAY MODEL STRUCTURE OF Fc(WT)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 22



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX

GRAY MODEL STRUCTURE OF Fc(WT)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 23

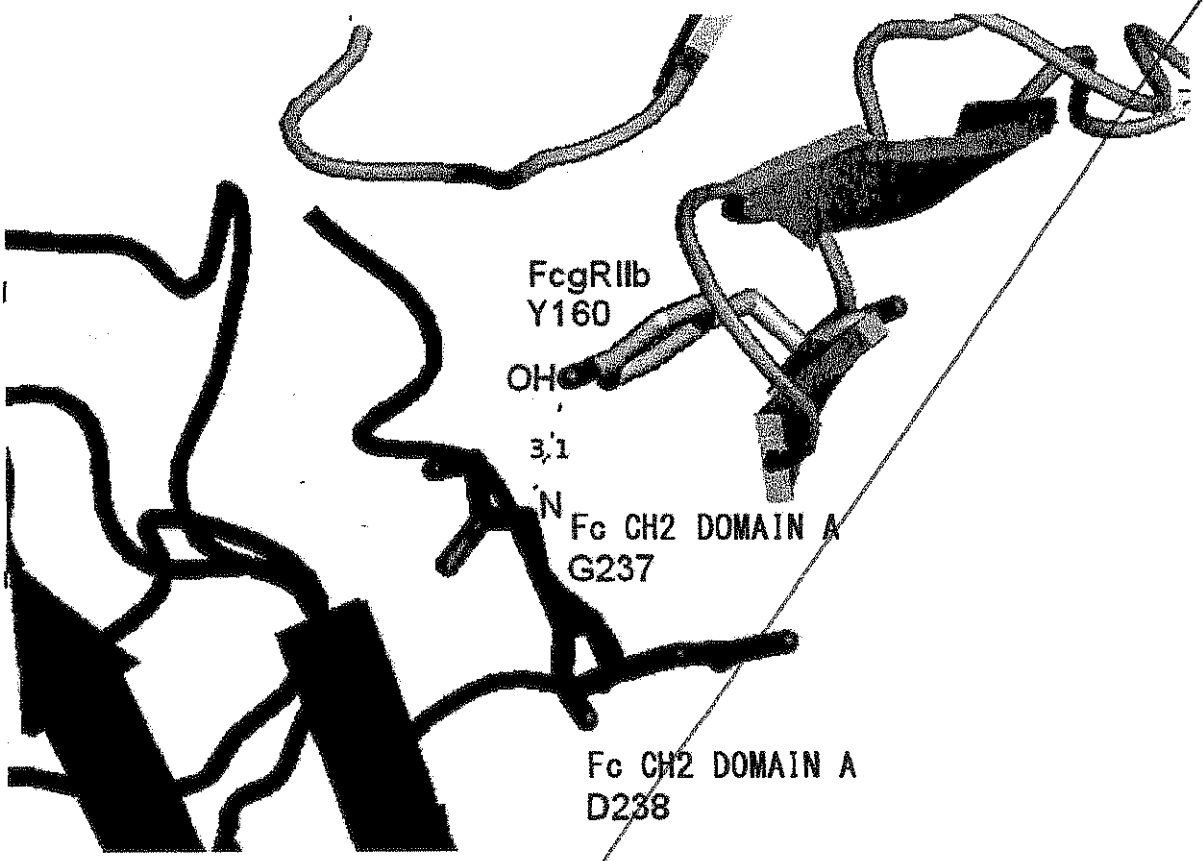


FIG. 24

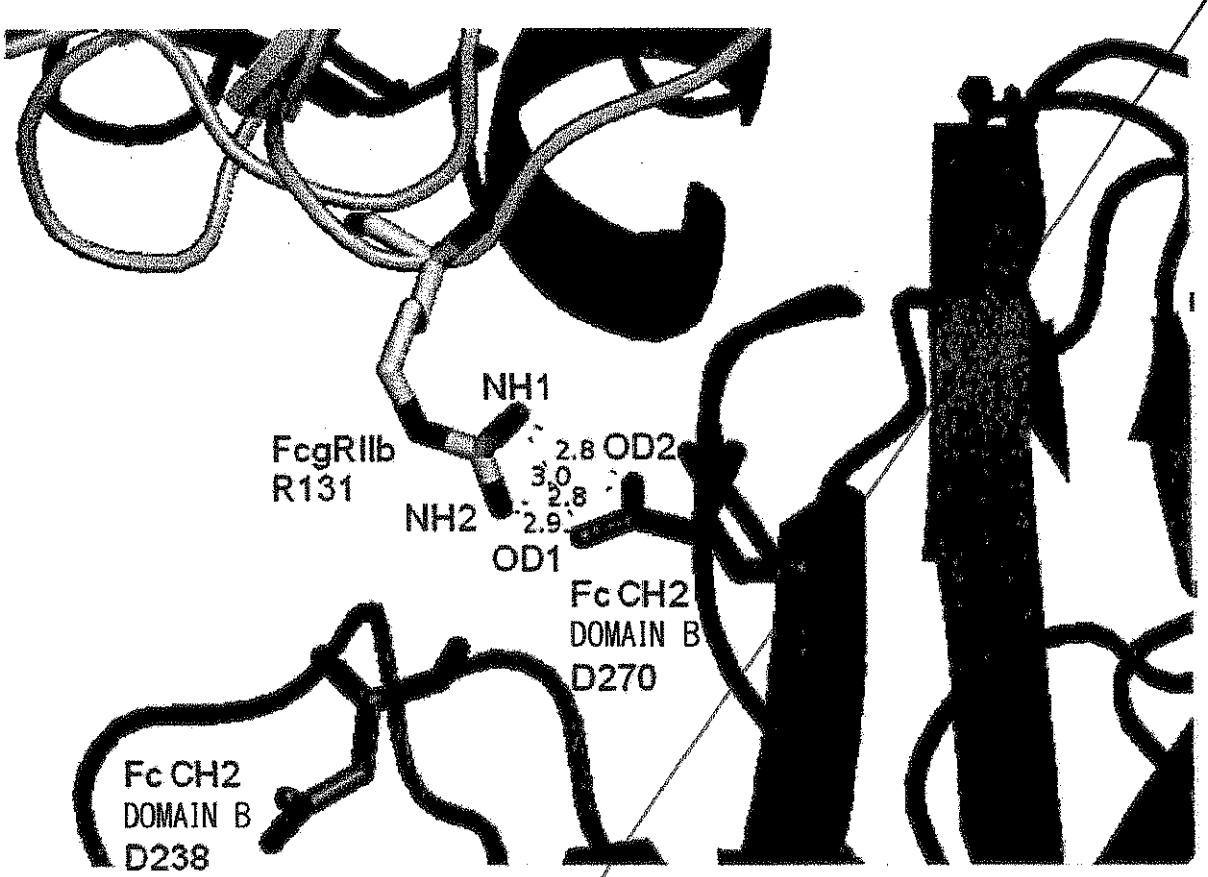

NH1
FcgRIIb
R131
2.8
OD2
3.0
2.8
NH2
2.9
OD1
Fc CH2
DOMAIN B
D270
Fc CH2
DOMAIN B
D238

FIG. 25

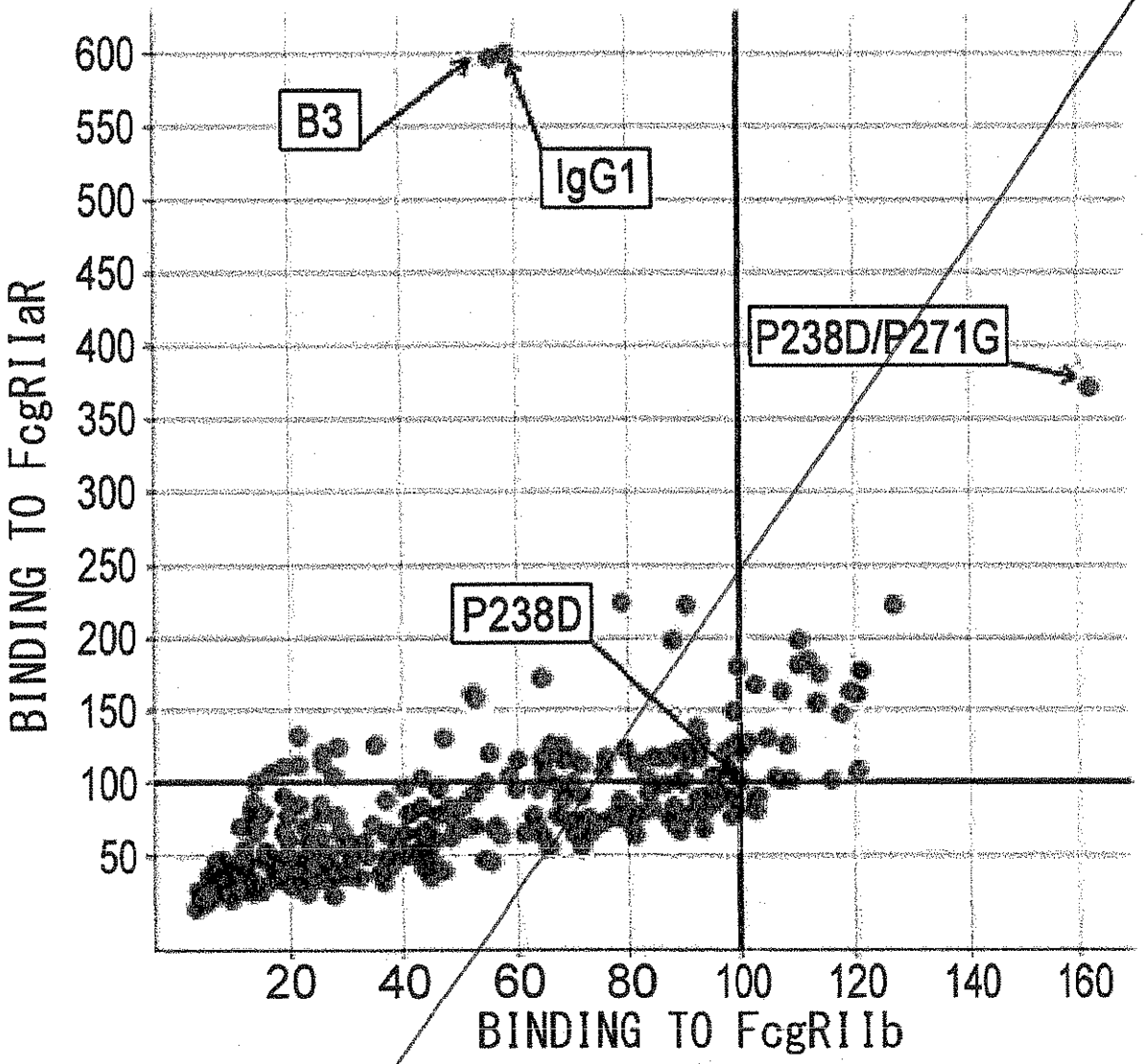

B3
IgG1
P238D/P271G
P238D
BINDING TO FcgRIIaR
BINDING TO FcgRIIb
600
550
500
450
400
350
300
250
200
150
100
50
20
40
60
80
100
120
140
160

FIG. 26

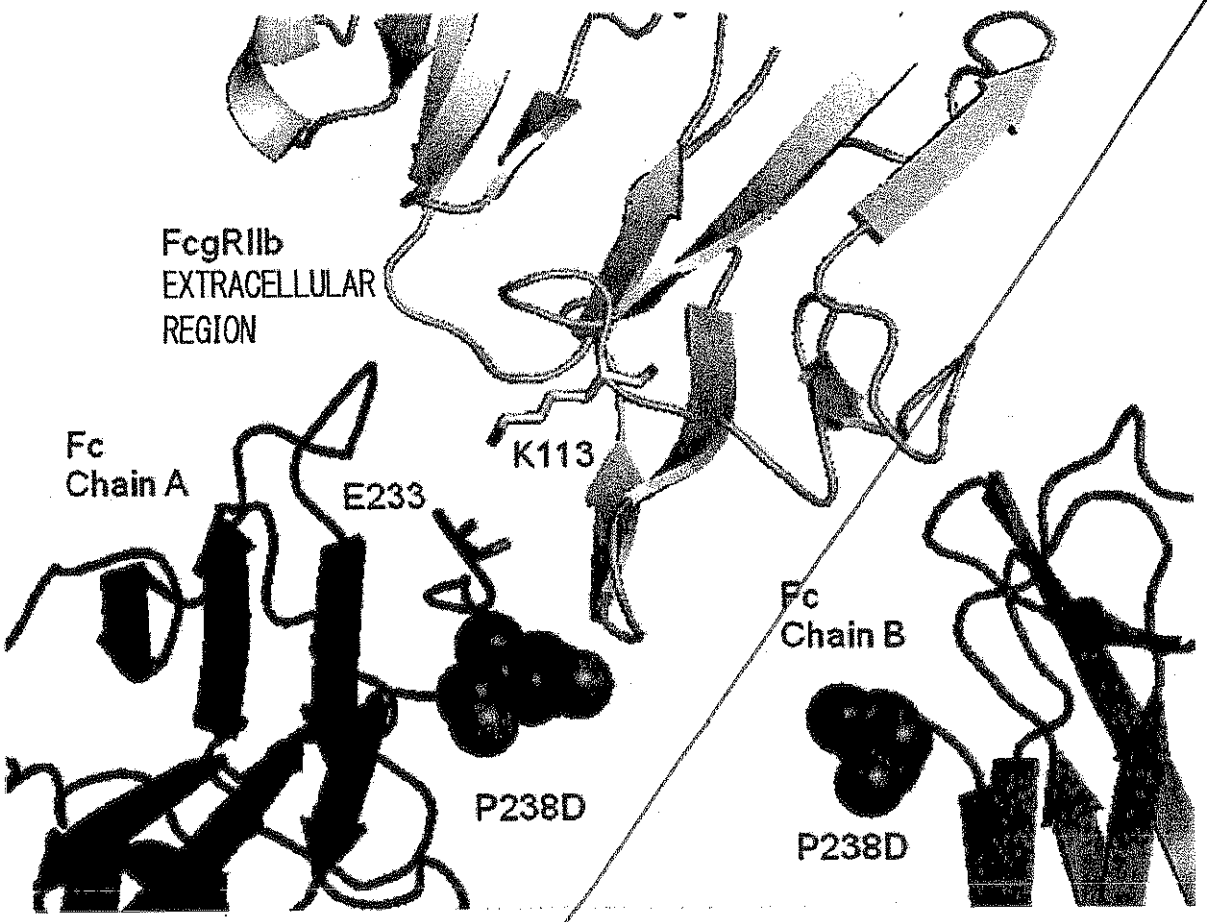

FcgRIIb
EXTRACELLULAR
REGION
Fc
Chain A
E233
K113
P238D
Fc
Chain B
P238D

FIG. 27

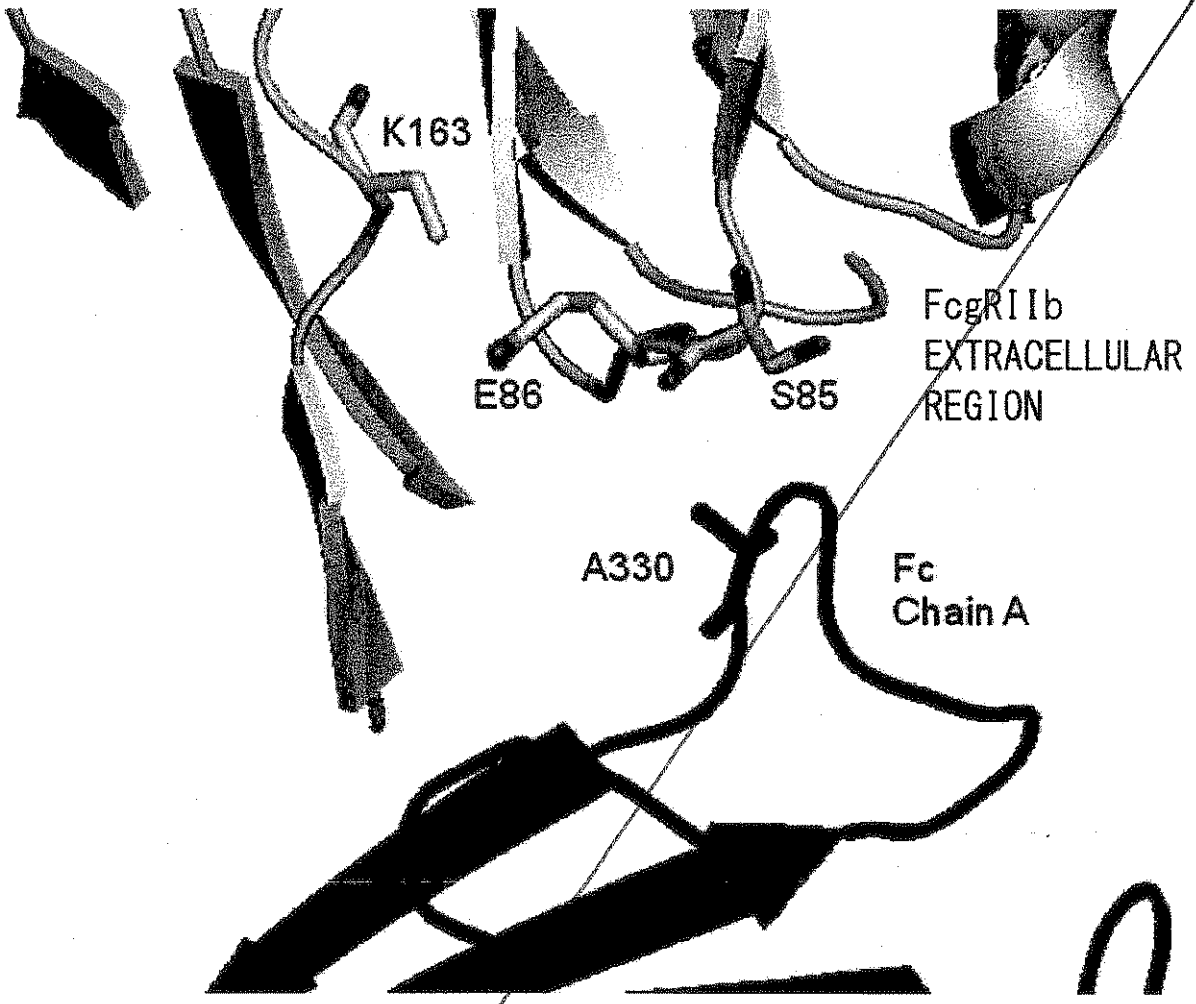
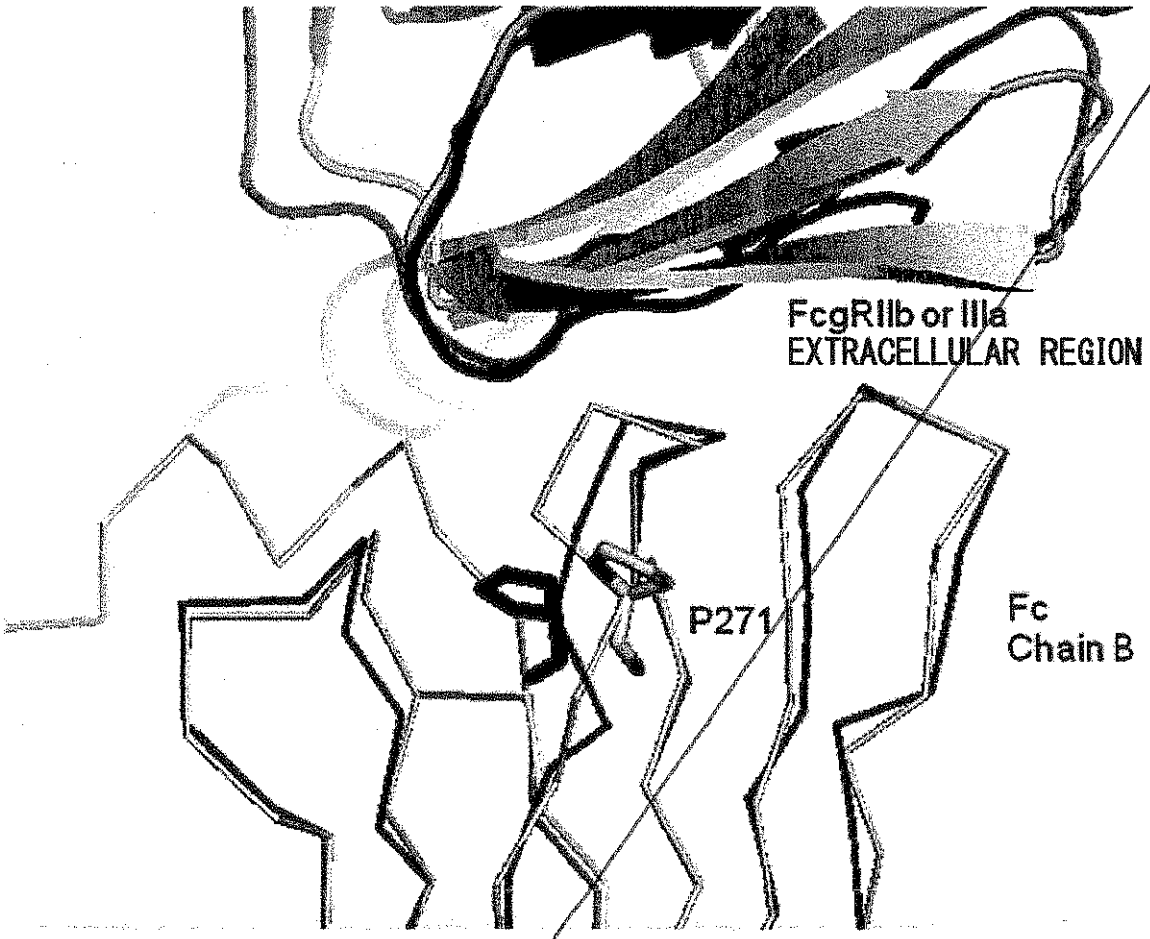


FIG. 28



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX
GRAY CRYSTAL STRUCTURE OF Fc(WT)/FcγRIIIa EXTRACELLULAR REGION COMPLEX (PDB code: 3SGJ)

FIG. 29

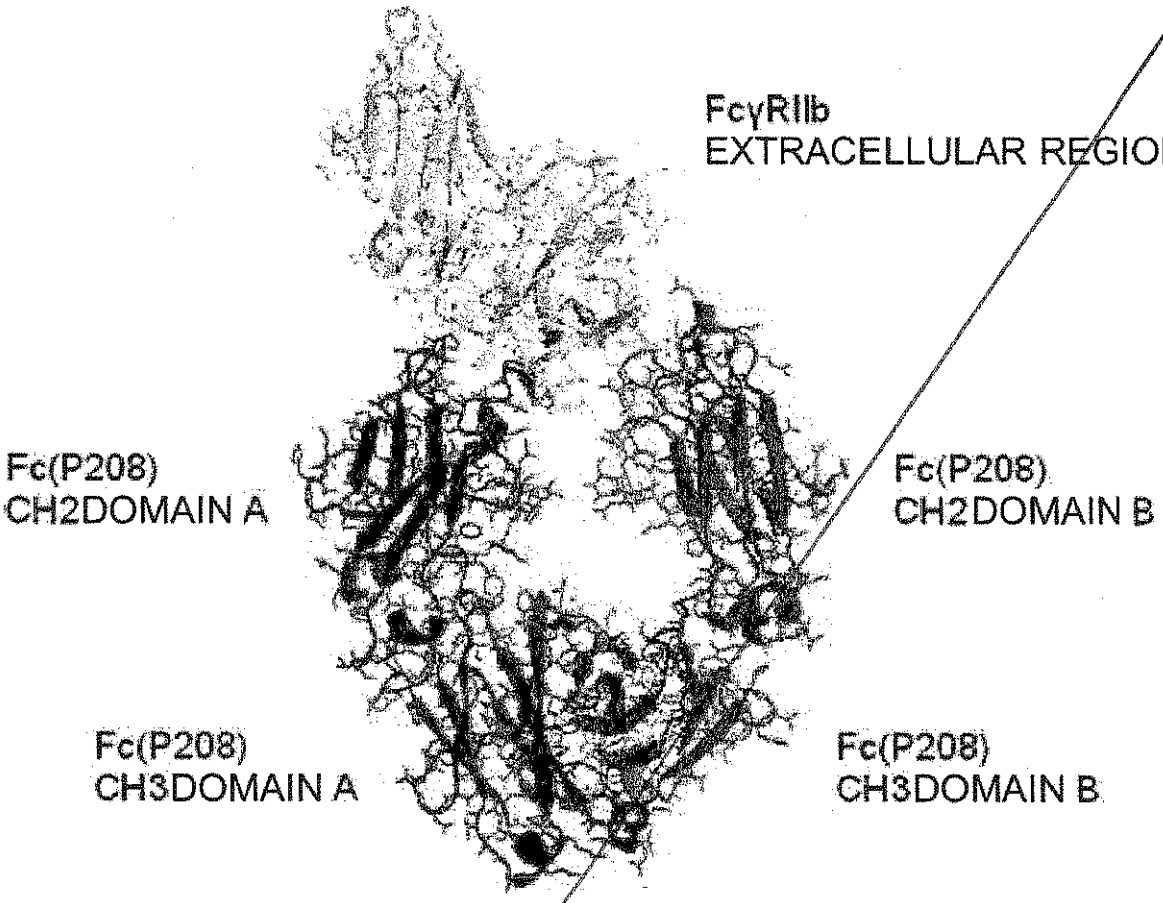
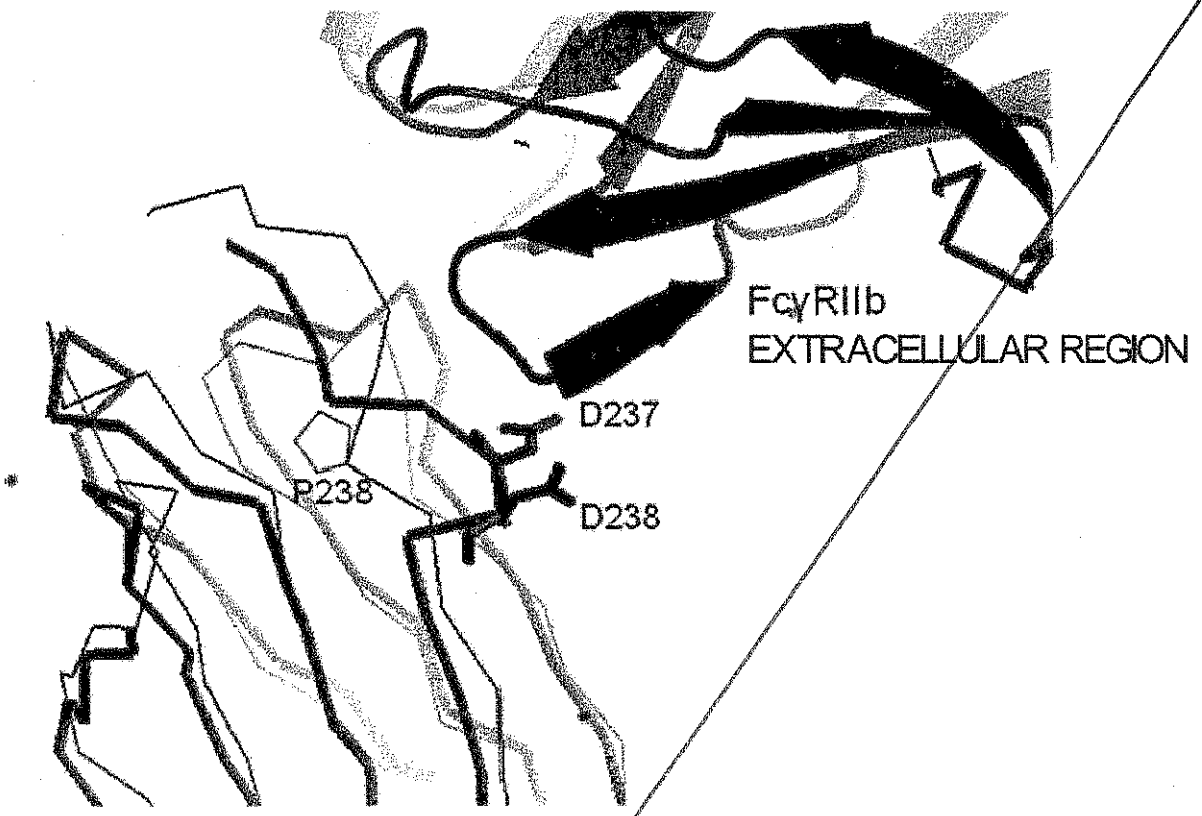

FcγRIIb
EXTRACELLULAR REGION
Fc(P208)
CH2DOMAIN A
Fc(P208)
CH2DOMAIN B
Fc(P208)
CH3DOMAIN A
Fc(P208)
CH3DOMAIN B

FIG. 30



THIN LINE: Fc(Wt) CH2DOMAIN A
HEAVY LINE: Fc(P208) CH2DOMAIN A

FIG. 31

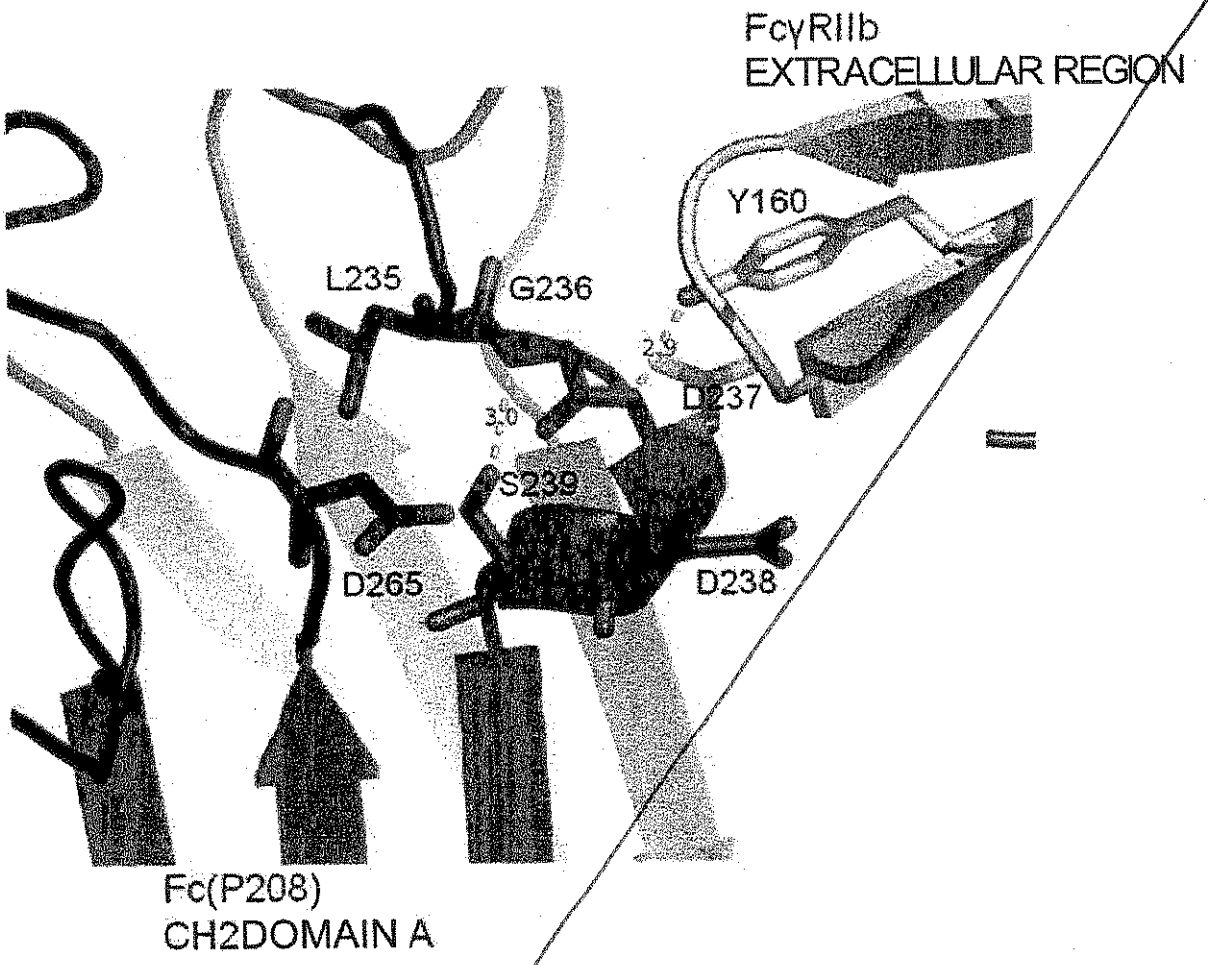

FcγRIIb
EXTRACELLULAR REGION
Y160
L235
G236
2.9
D237
3.0
S239
D265
D238
Fc(P208)
CH2DOMAIN A

FIG. 32

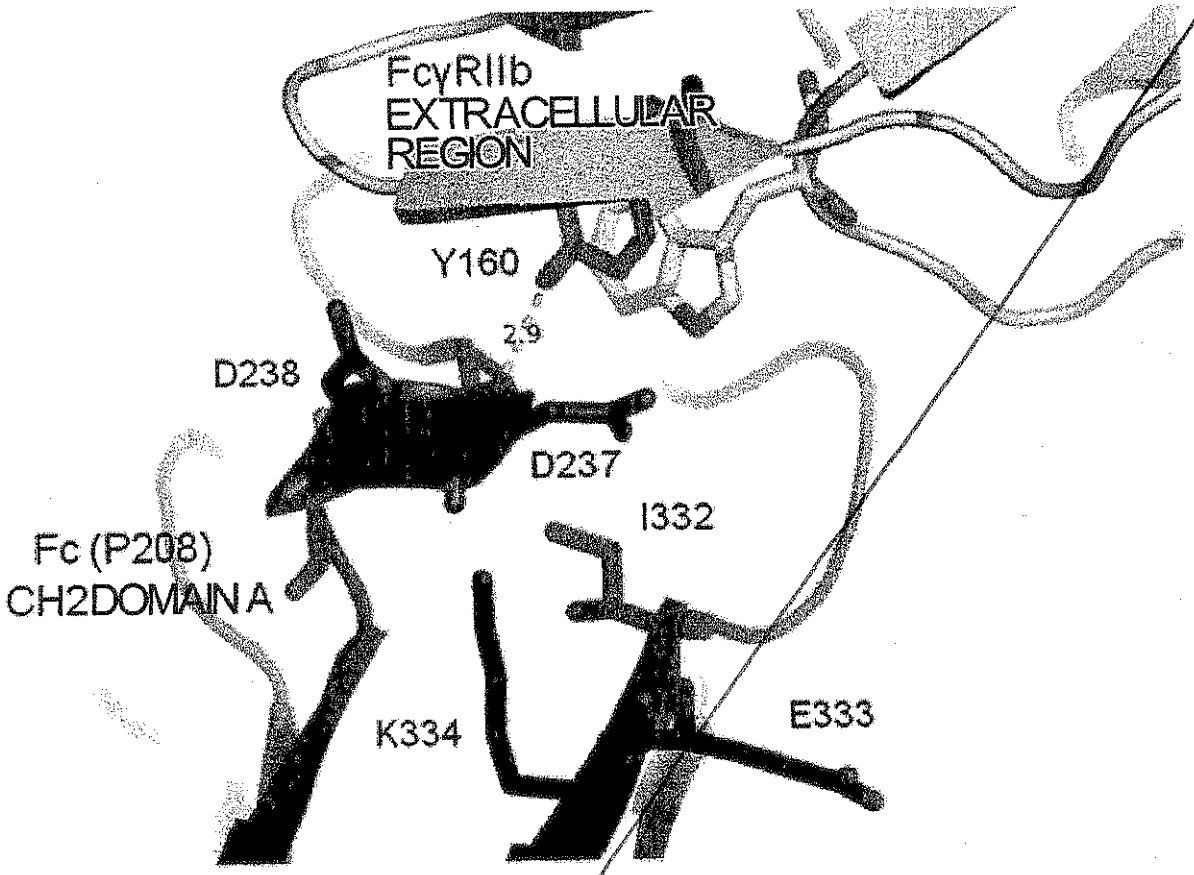
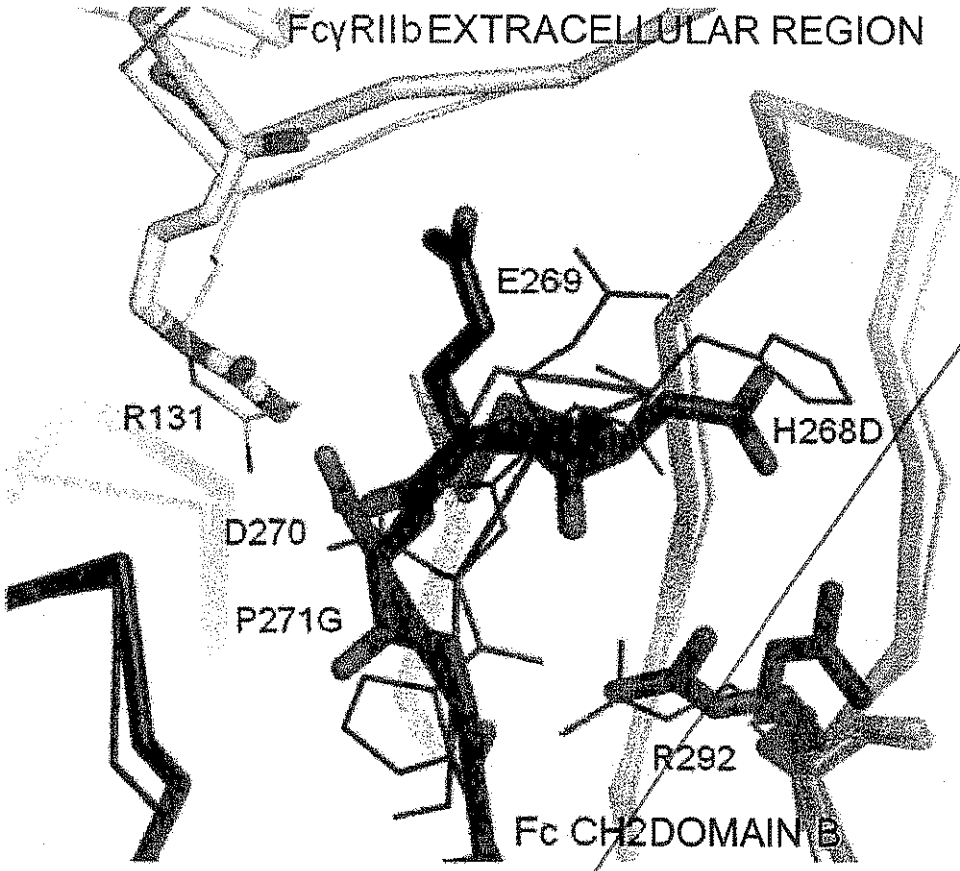
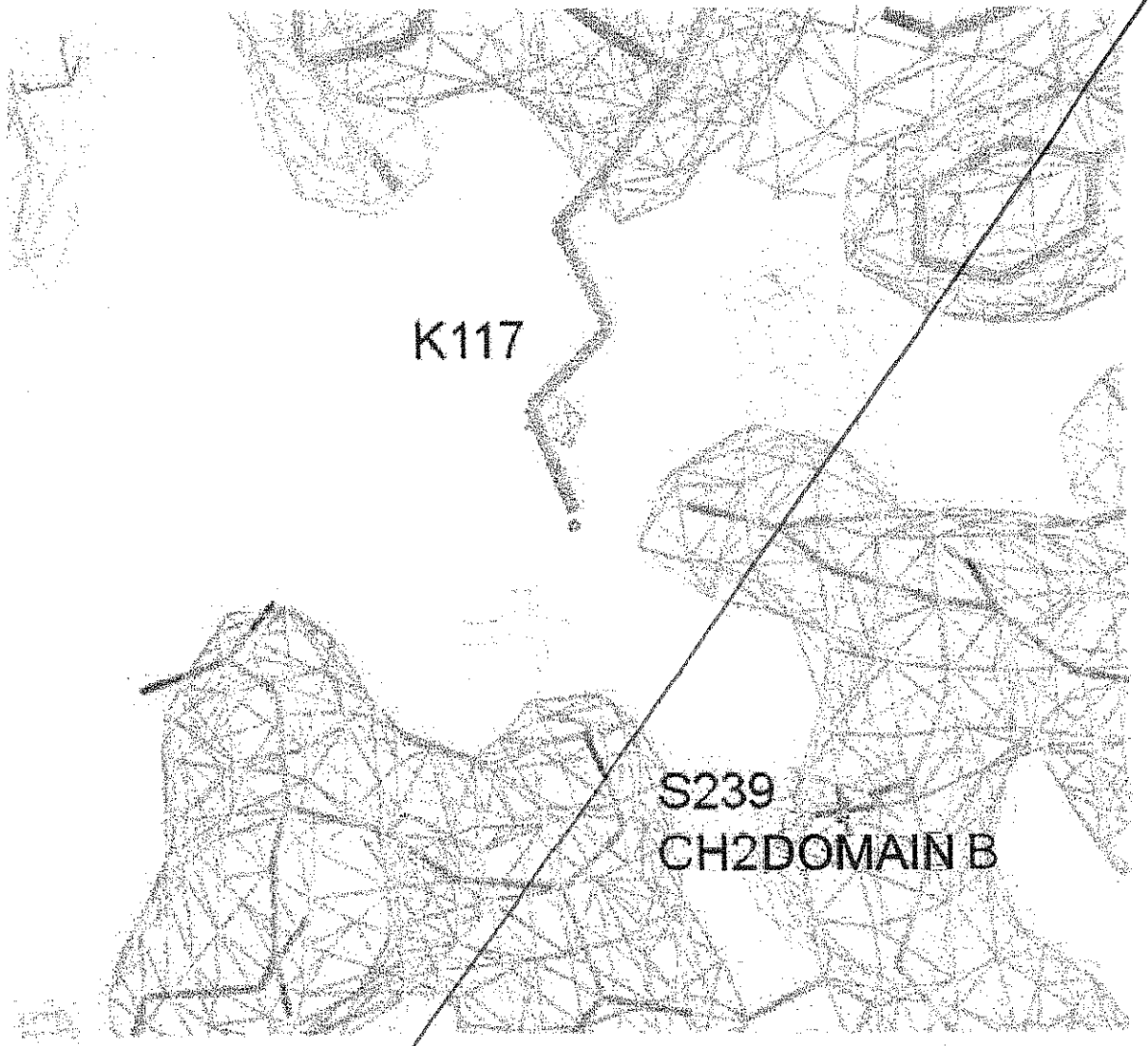

FcγRIIb
EXTRACELLULAR
REGION
Y160
2.9
D238
D237
I332
Fc (P208)
CH2DOMAIN A
K334
E333

FIG. 33



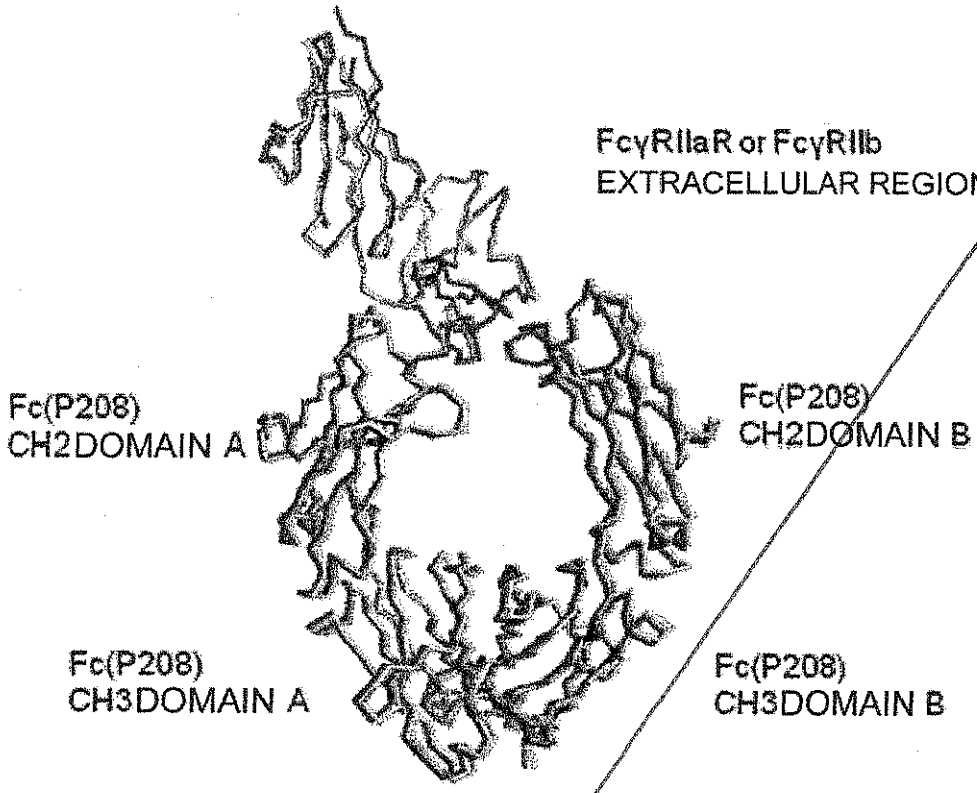
THIN LINE: X-RAY CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX
HEAVY LINE: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 34



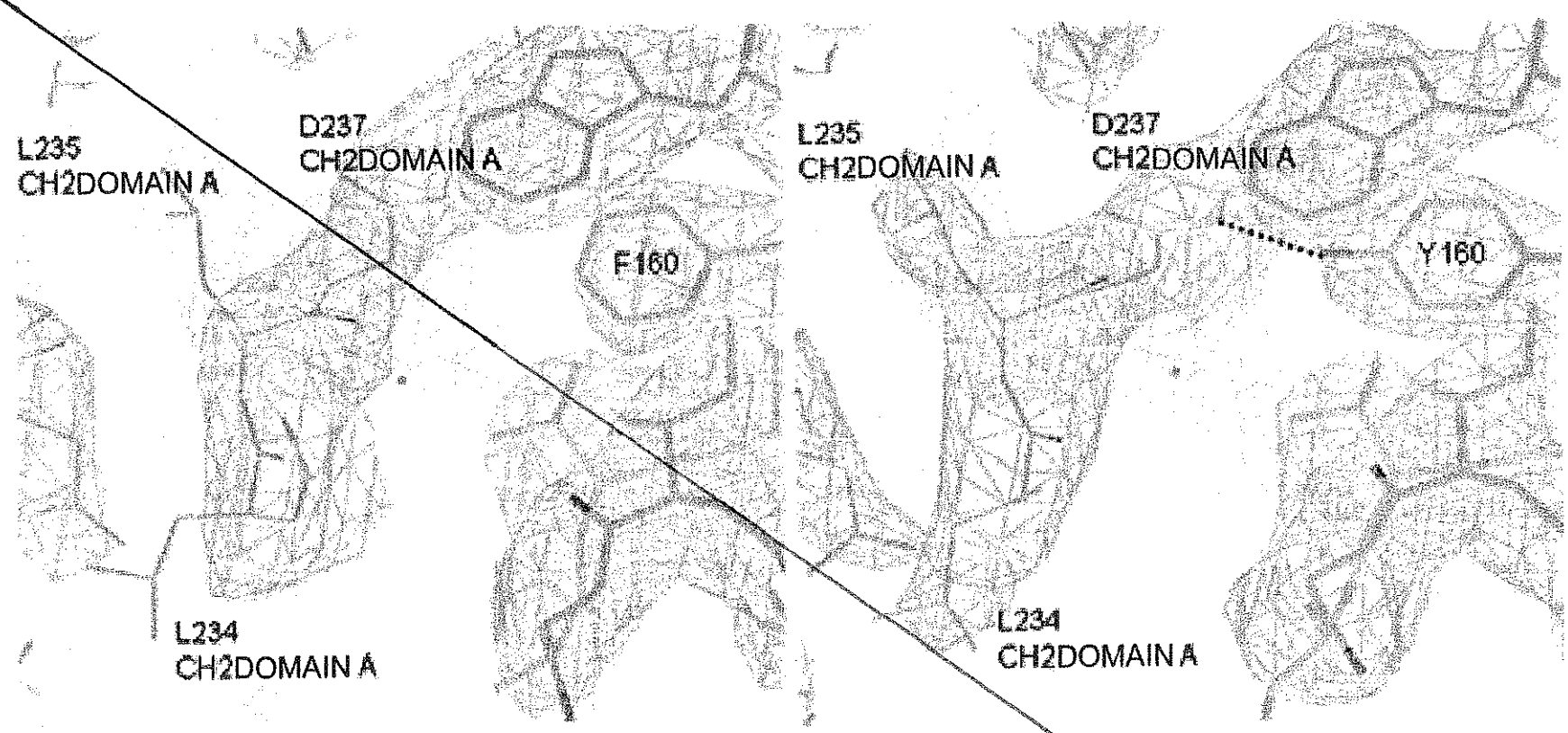
THIN LINE : Fc(P208)
HEAVY LINE : FcγRIIb EXTRACELLULAR REGION

FIG. 35



BLACK: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX
GRAY: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 36



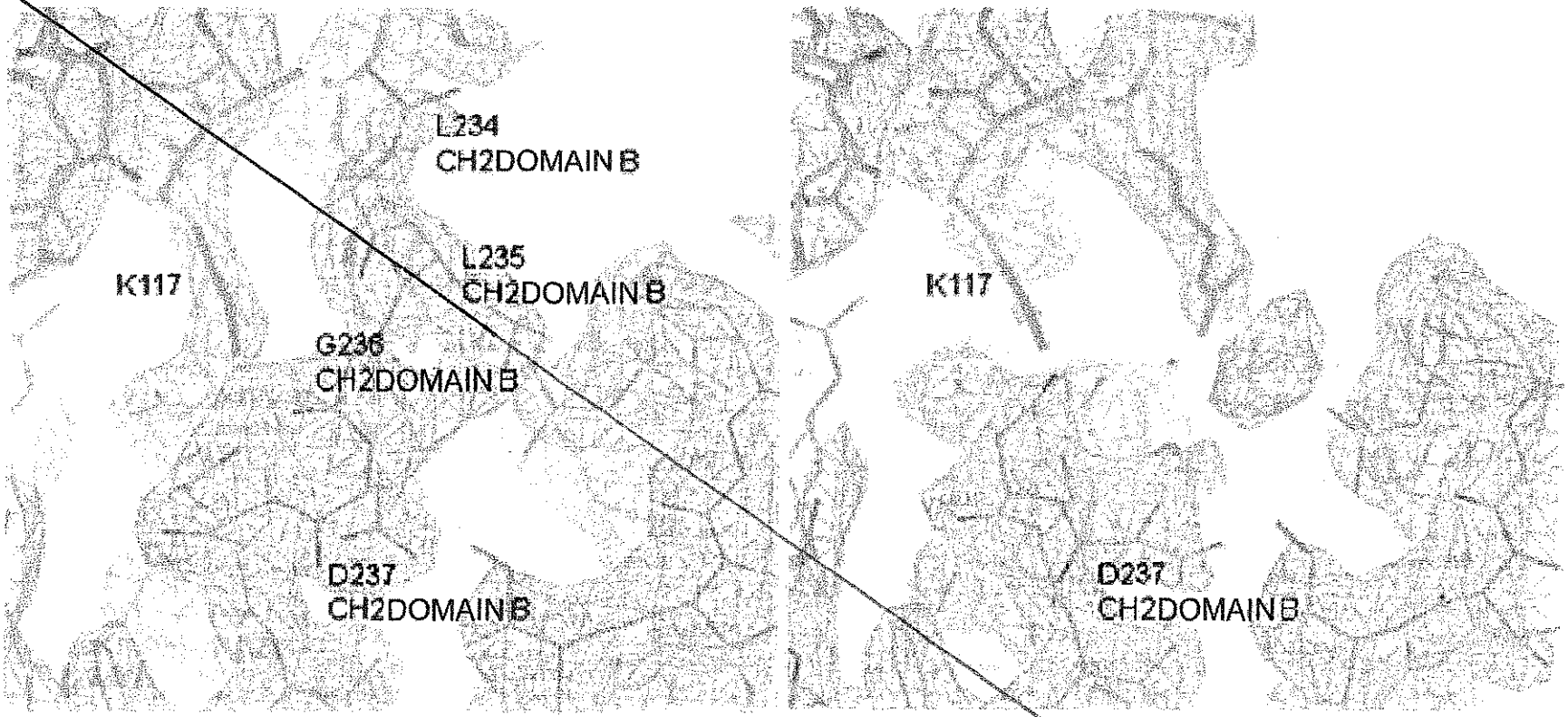
THIN LINE: Fc(P208)

HEAVY LINE: FcγRIIaR or FcγRIIb EXTRACELLULAR REGION

LEFT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX

RIGHT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 37



THIN LINE: Fc(P208)

HEAVY LINE: FcγRIIaR or FcγRIIb EXTRACELLULAR REGION

LEFT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX

RIGHT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 38

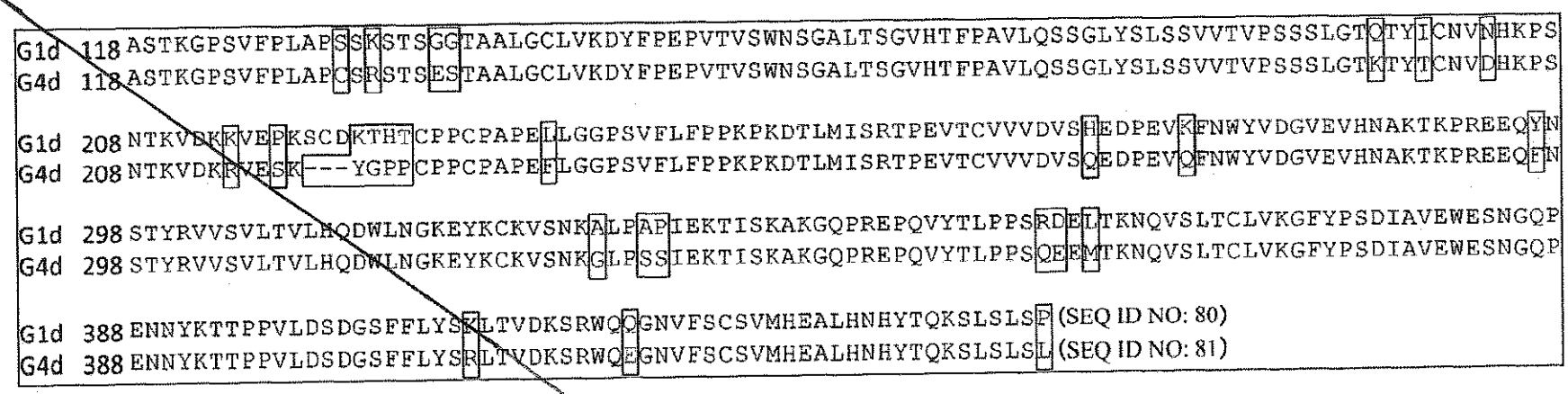

G1d 118 ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
G4d 118 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPS
G1d 208 NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
G4d 208 NTKVDKRVESK---YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN
G1d 298 STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
G4d 298 STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
G1d 388 ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 80)
G4d 388 ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSL (SEQ ID NO: 81)

FIG. 39

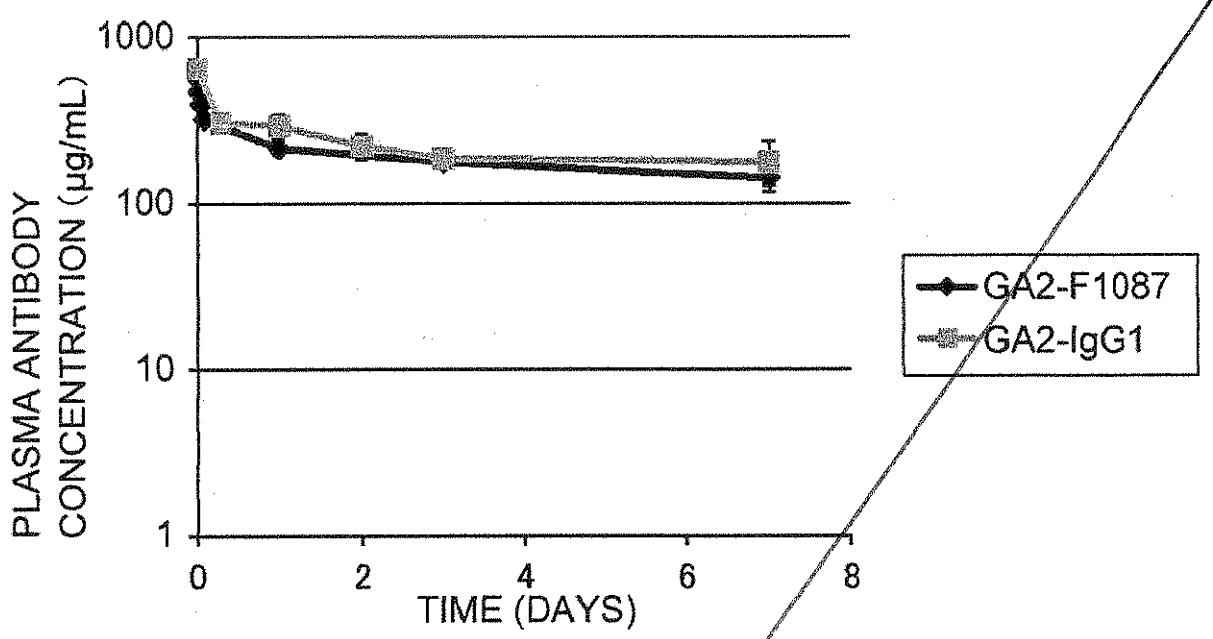

1000
100
10
1
PLASMA ANTIBODY CONCENTRATION (µg/mL)
0
2
4
6
8
TIME (DAYS)
GA2-F1087
GA2-IgG1

FIG. 40

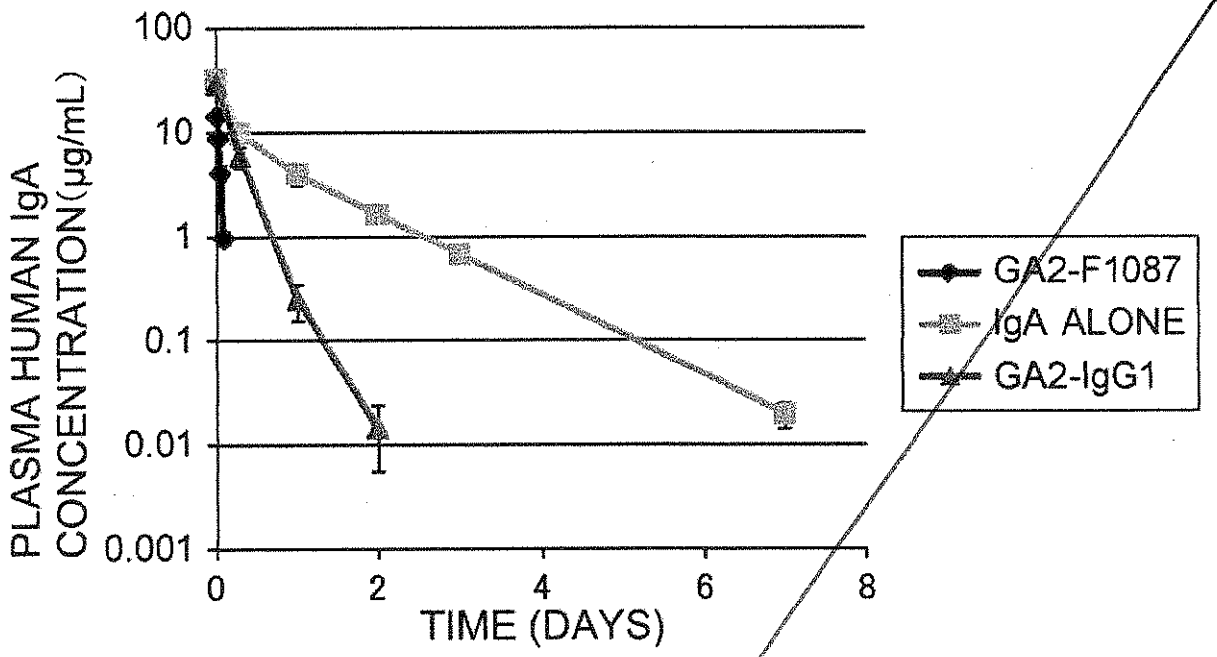

100
10
1
0.1
0.01
0.001
PLASMA HUMAN IgA CONCENTRATION(µg/mL)
0
2
4
6
8
TIME (DAYS)
GA2-F1087
IgA ALONE
GA2-IgG1

FIG. 41

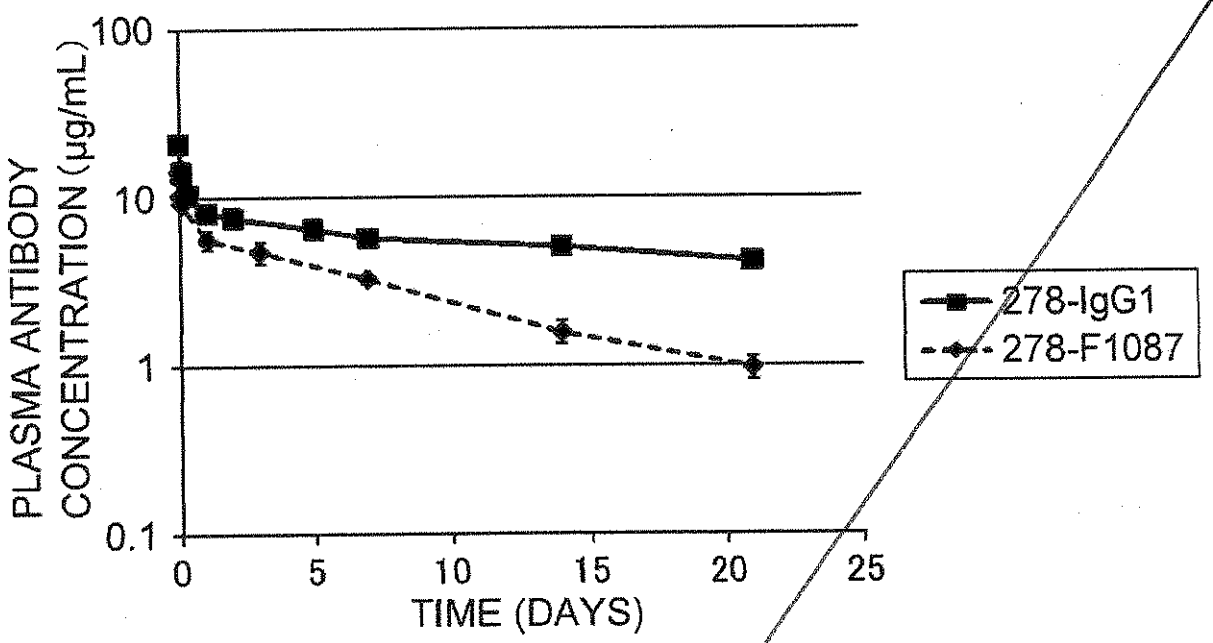

PLASMA ANTIBODY CONCENTRATION (µg/mL)
100
10
1
0.1
0
5
10
15
20
25
TIME (DAYS)
278-IgG1
278-F1087

FIG. 42

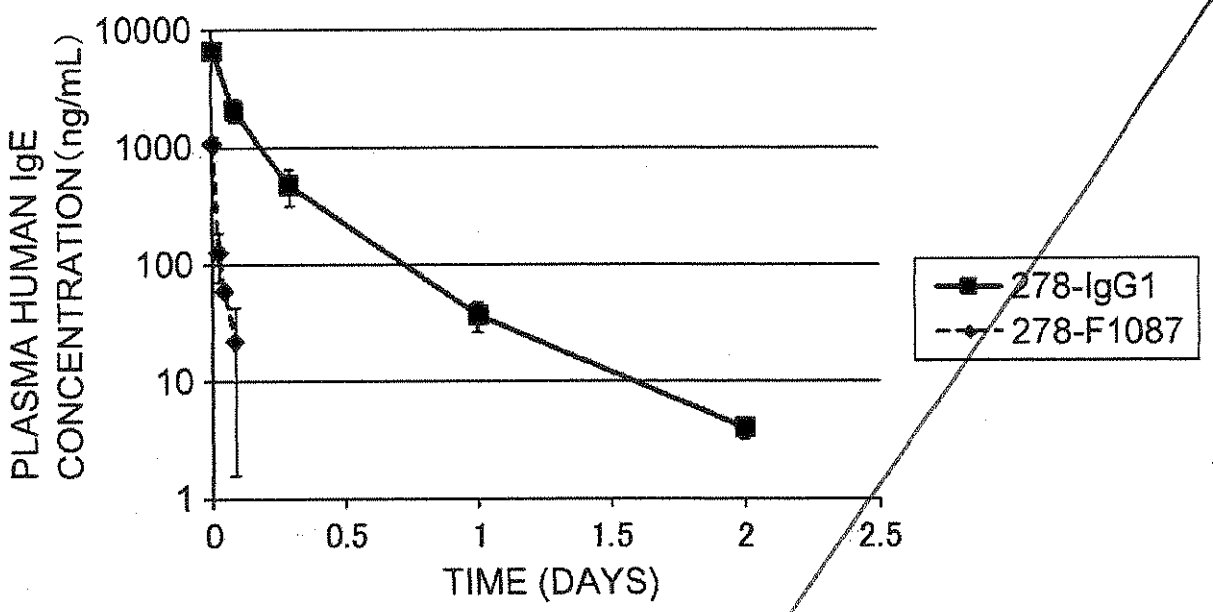

PLASMA HUMAN IgE CONCENTRATION (ng/mL)
10000
1000
100
10
1
0
0.5
1
1.5
2
2.5
TIME (DAYS)
278-IgG1
278-F1087

FIG. 43

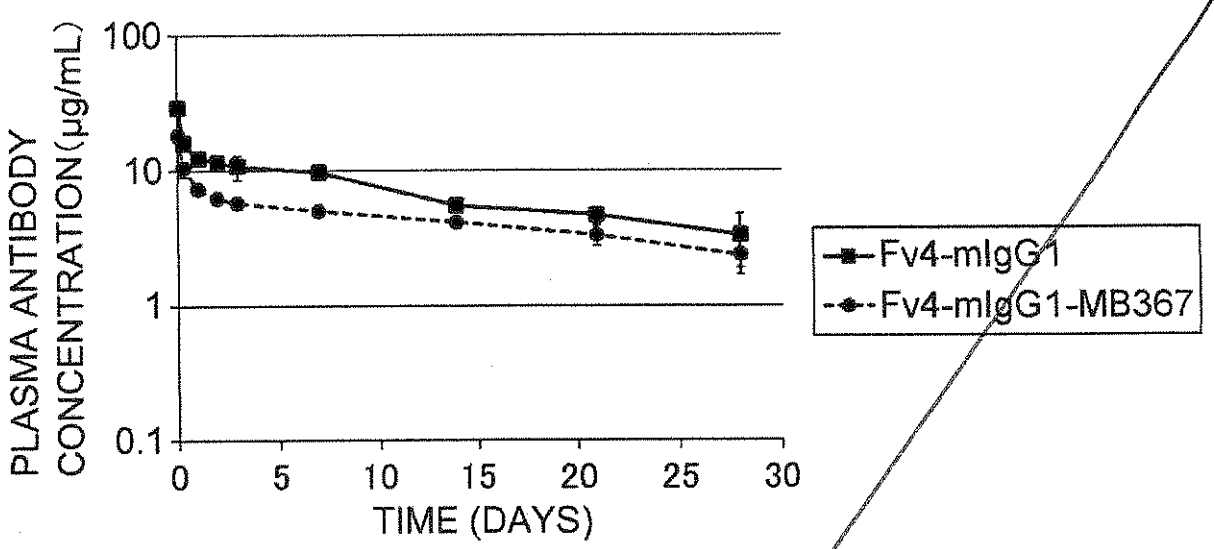

PLASMA ANTIBODY CONCENTRATION(μg/mL)
100
10
1
0.1
0
5
10
15
20
25
30
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-MB367

FIG. 44

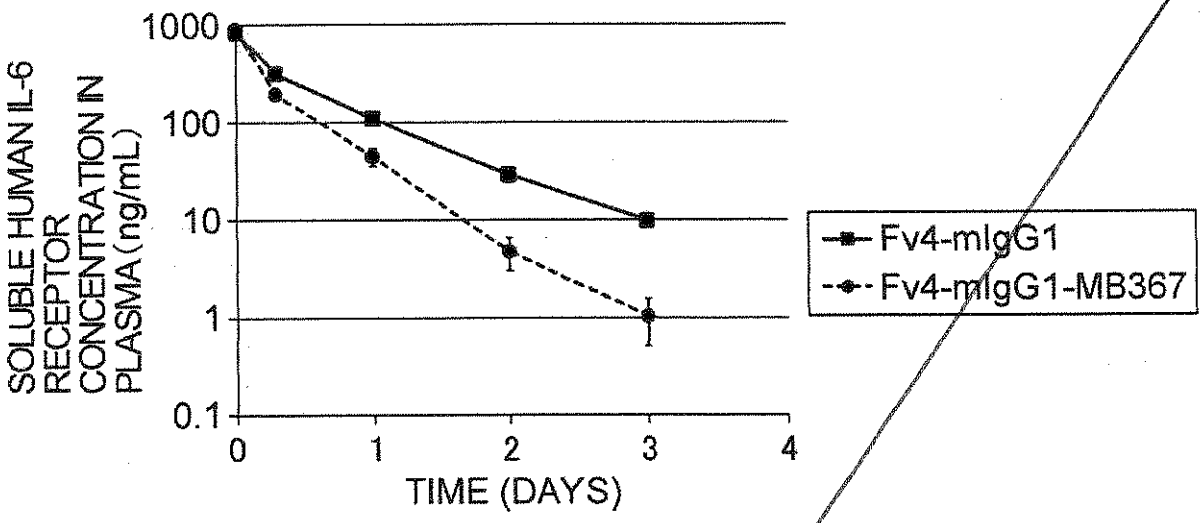

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-MB367

FIG. 45

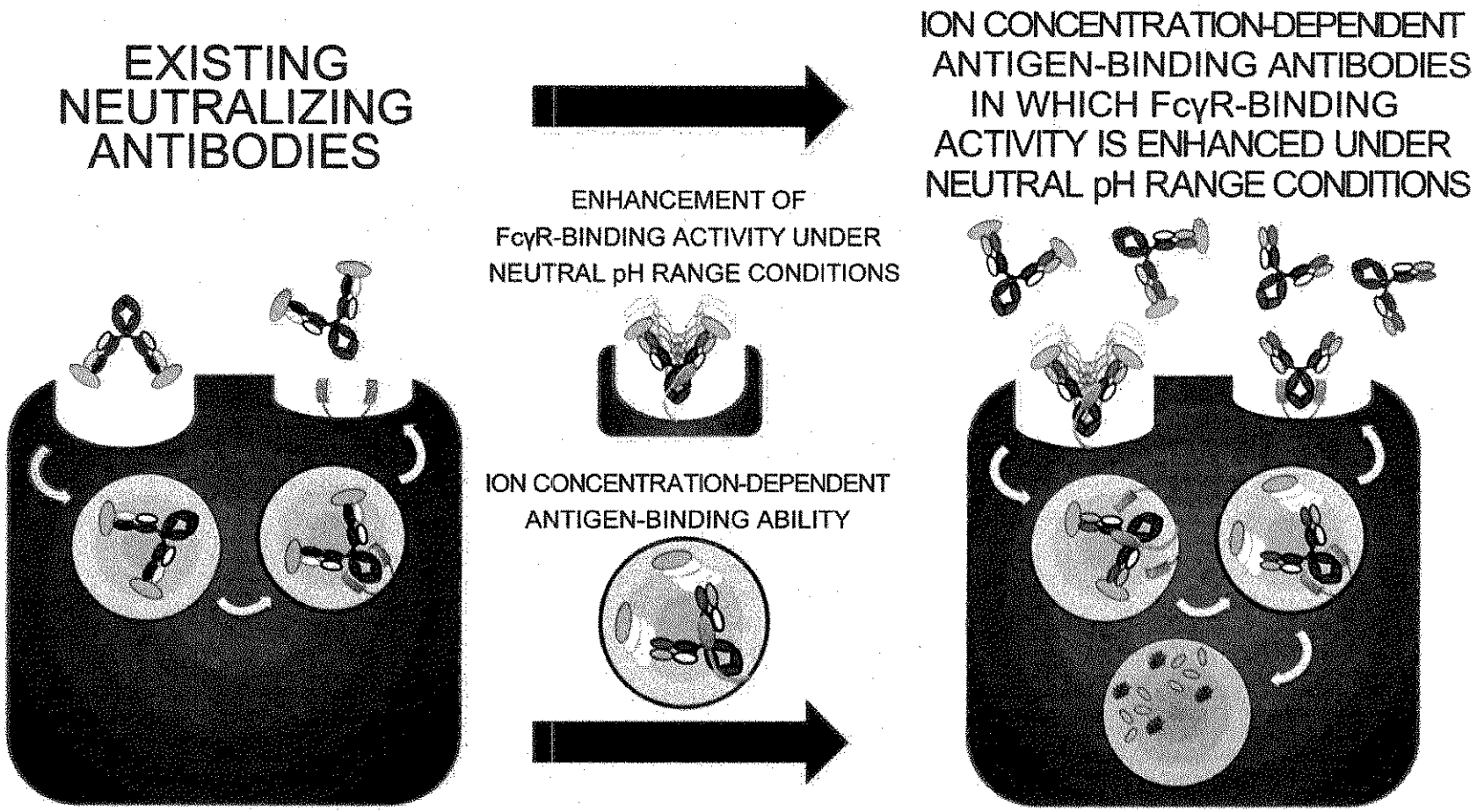

EXISTING NEUTRALIZING ANTIBODIES
ENHANCEMENT OF FcγR-BINDING ACTIVITY UNDER NEUTRAL pH RANGE CONDITIONS
ION CONCENTRATION-DEPENDENT ANTIGEN-BINDING ABILITY
ION CONCENTRATION-DEPENDENT ANTIGEN-BINDING ANTIBODIES IN WHICH FcγR-BINDING ACTIVITY IS ENHANCED UNDER NEUTRAL pH RANGE CONDITIONS

FIG. 1

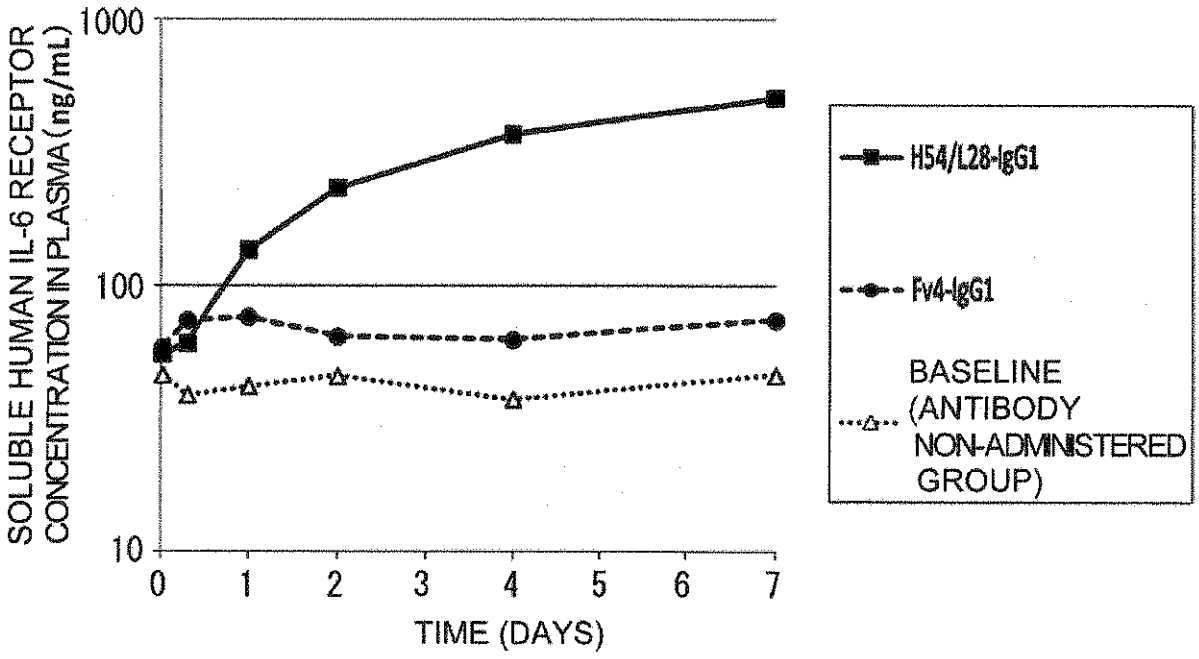

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
0
1
2
3
4
5
6
7
TIME (DAYS)
H54/L28-IgG1
Fv4-IgG1
BASELINE (ANTIBODY NON-ADMINISTERED GROUP)

FIG. 2

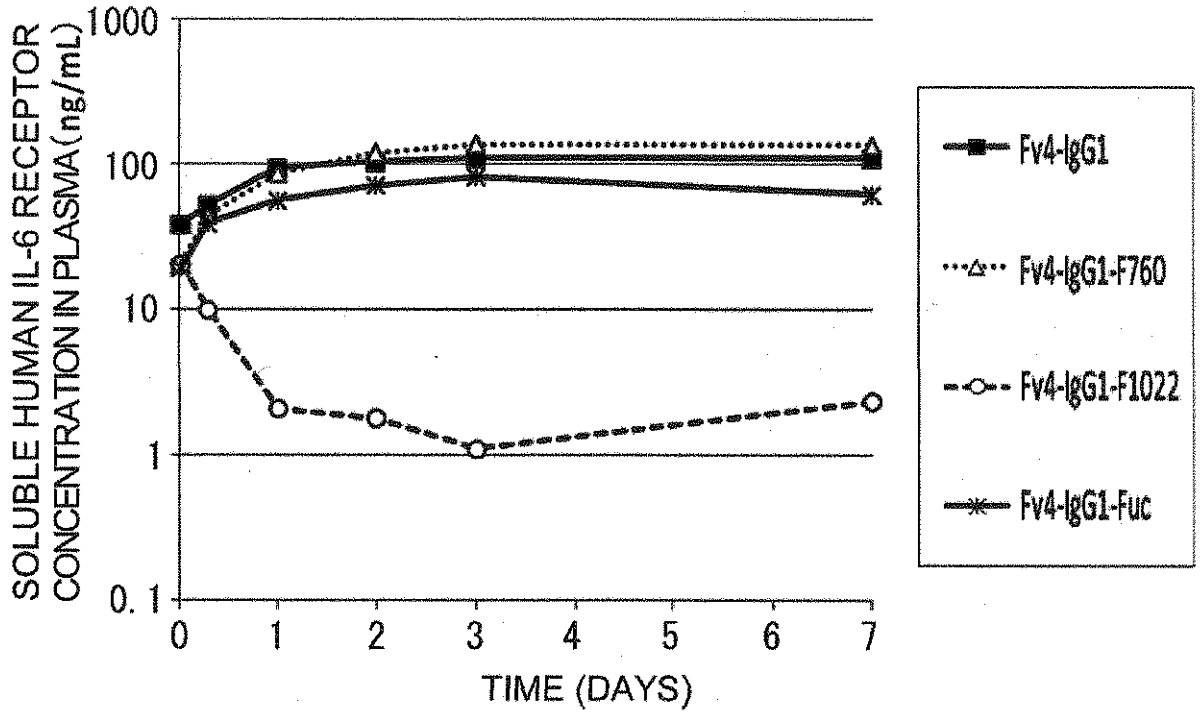

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F760
Fv4-IgG1-F1022
Fv4-IgG1-Fuc

FIG. 3

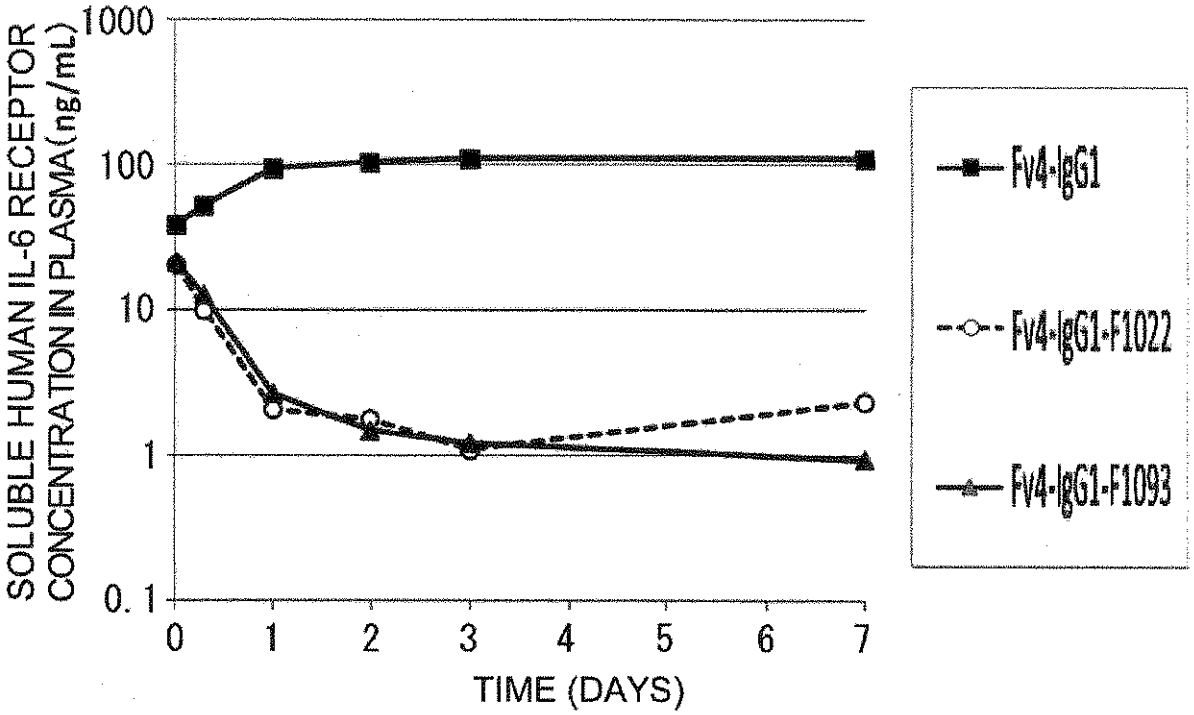

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1022
Fv4-IgG1-F1093

FIG. 4

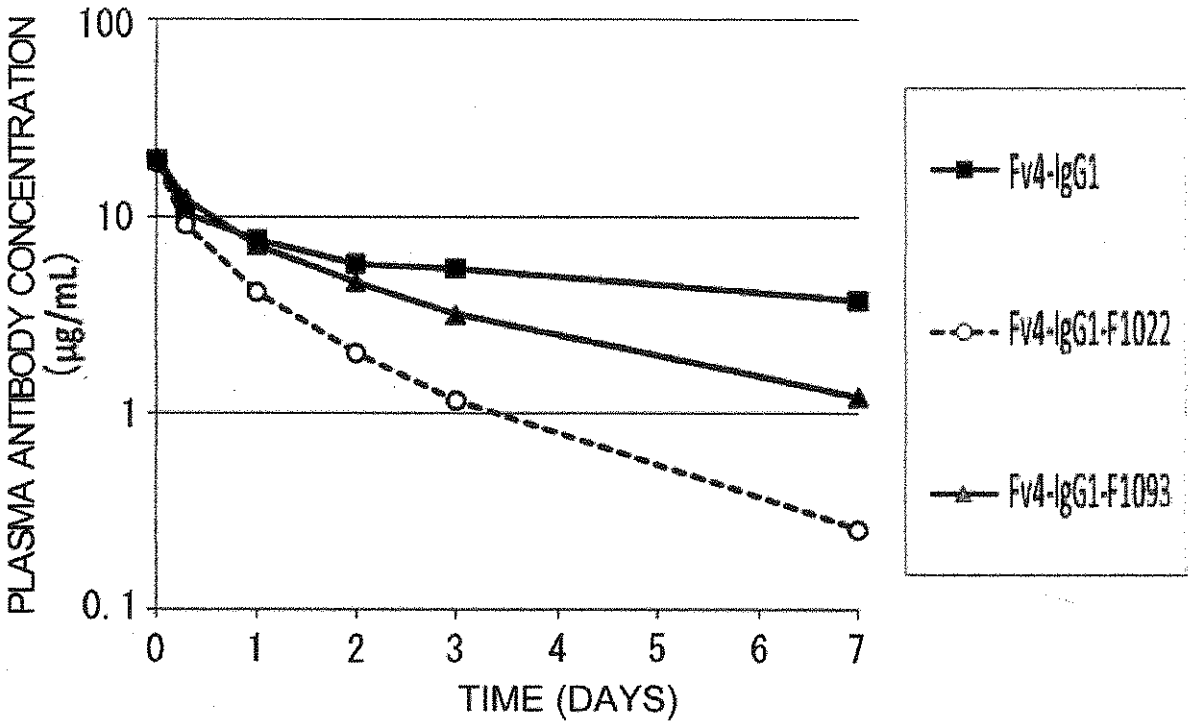

PLASMA ANTIBODY CONCENTRATION (μg/mL)
100
10
1
0.1
0
1
2
3
4
5
6
7
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1022
Fv4-IgG1-F1093

FIG. 5

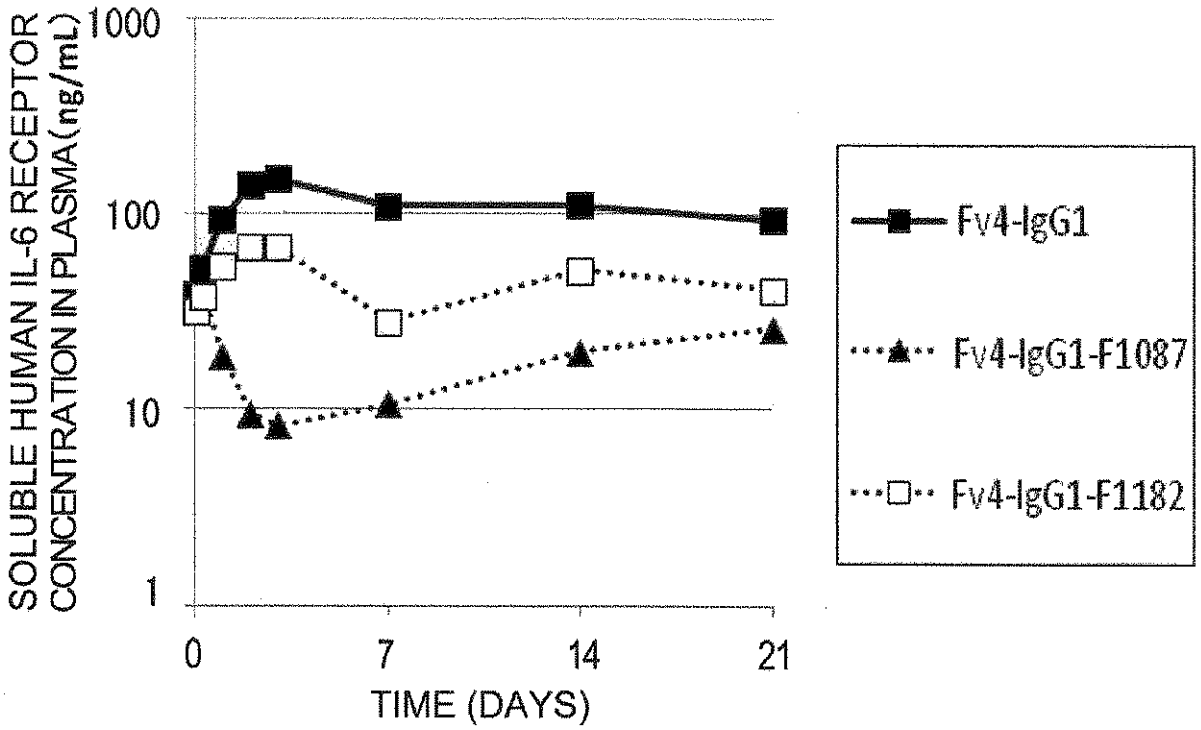

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1182

FIG. 6

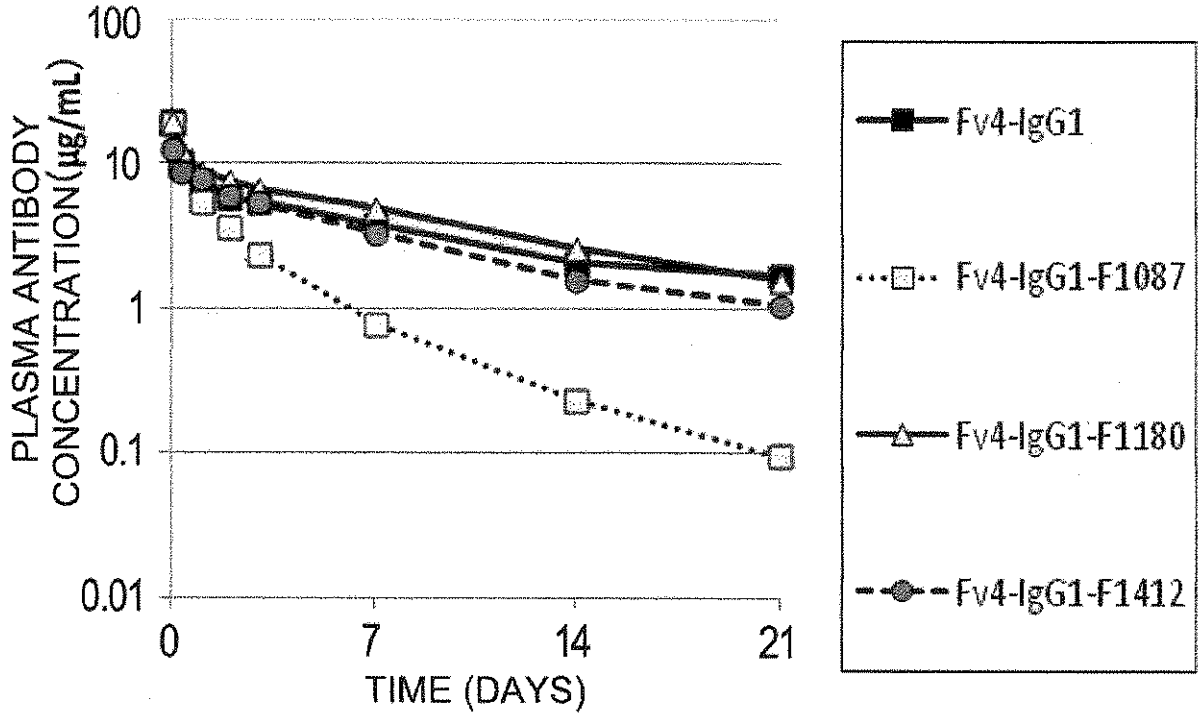

100
10
1
0.1
0.01
PLASMA ANTIBODY CONCENTRATION(μg/mL)
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1180
Fv4-IgG1-F1412

FIG. 7

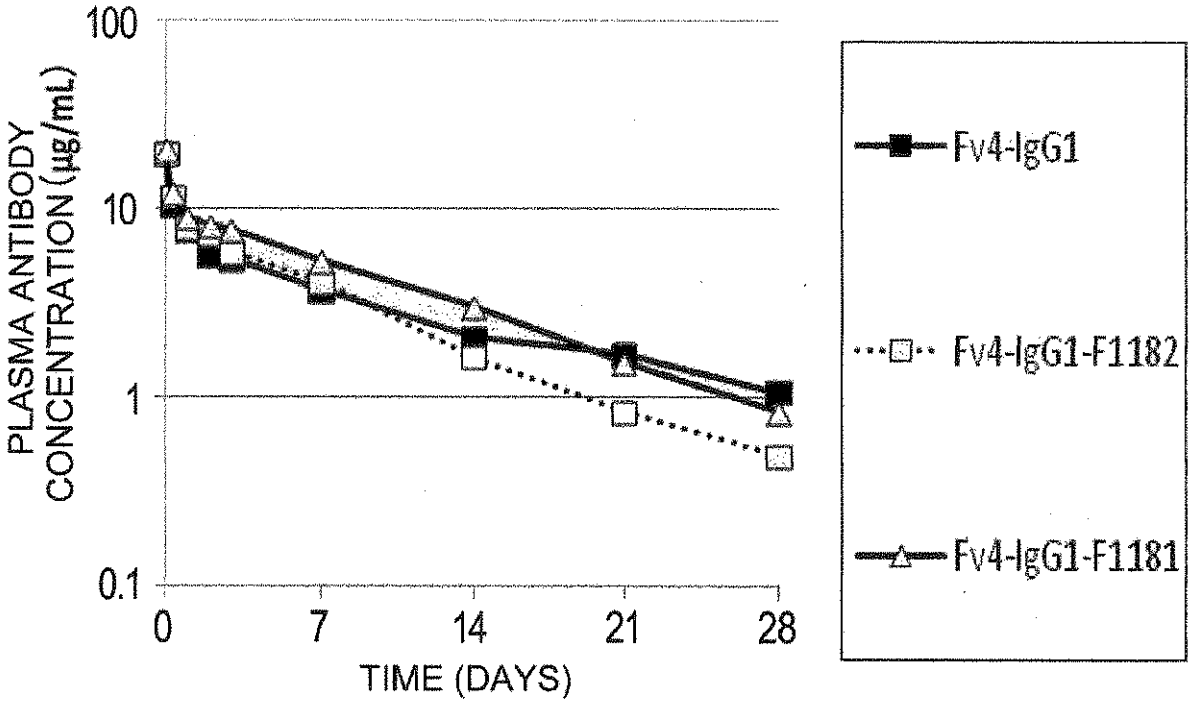

100
10
1
0.1
PLASMA ANTIBODY CONCENTRATION (μg/mL)
0
7
14
21
28
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1182
Fv4-IgG1-F1181

FIG. 8

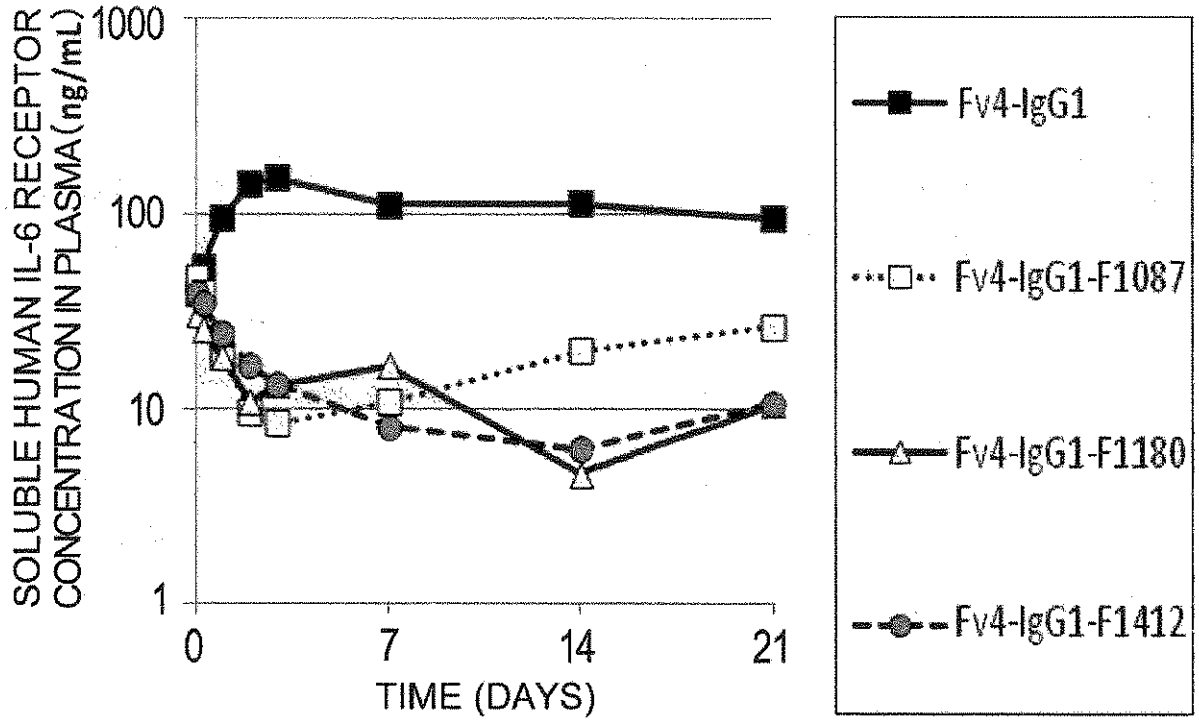

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1087
Fv4-IgG1-F1180
Fv4-IgG1-F1412

FIG. 9

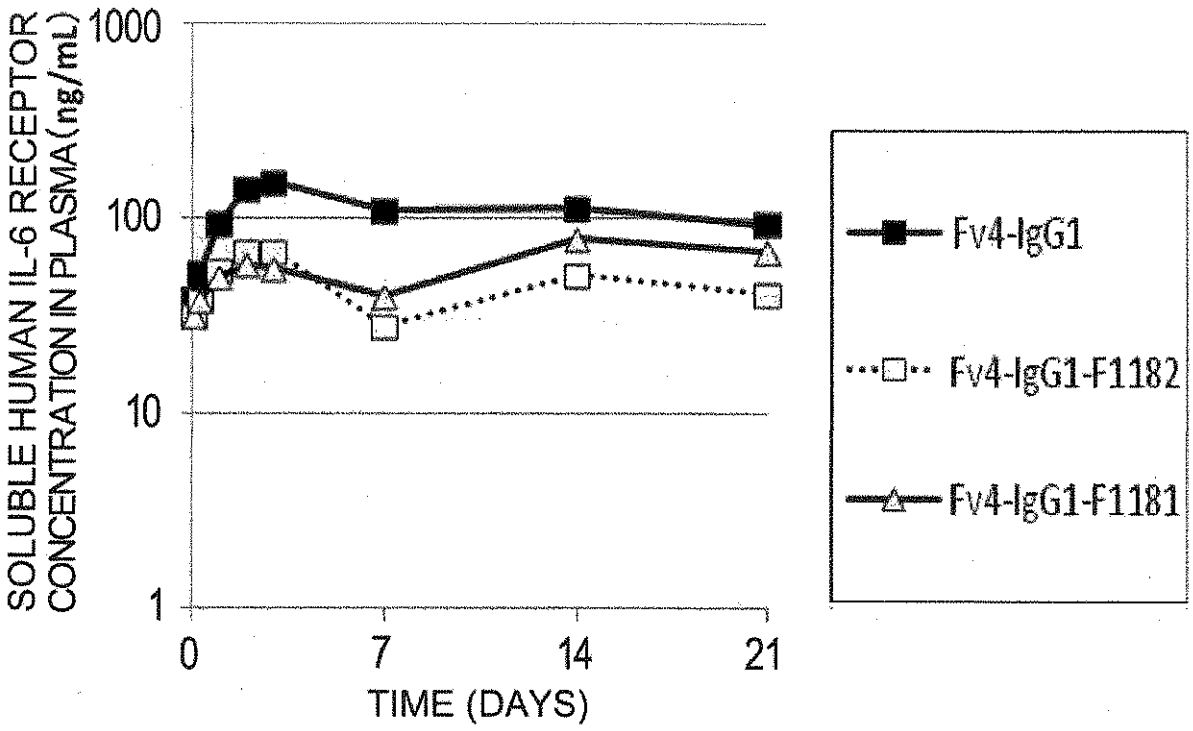

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-IgG1
Fv4-IgG1-F1182
Fv4-IgG1-F1181

FIG. 10

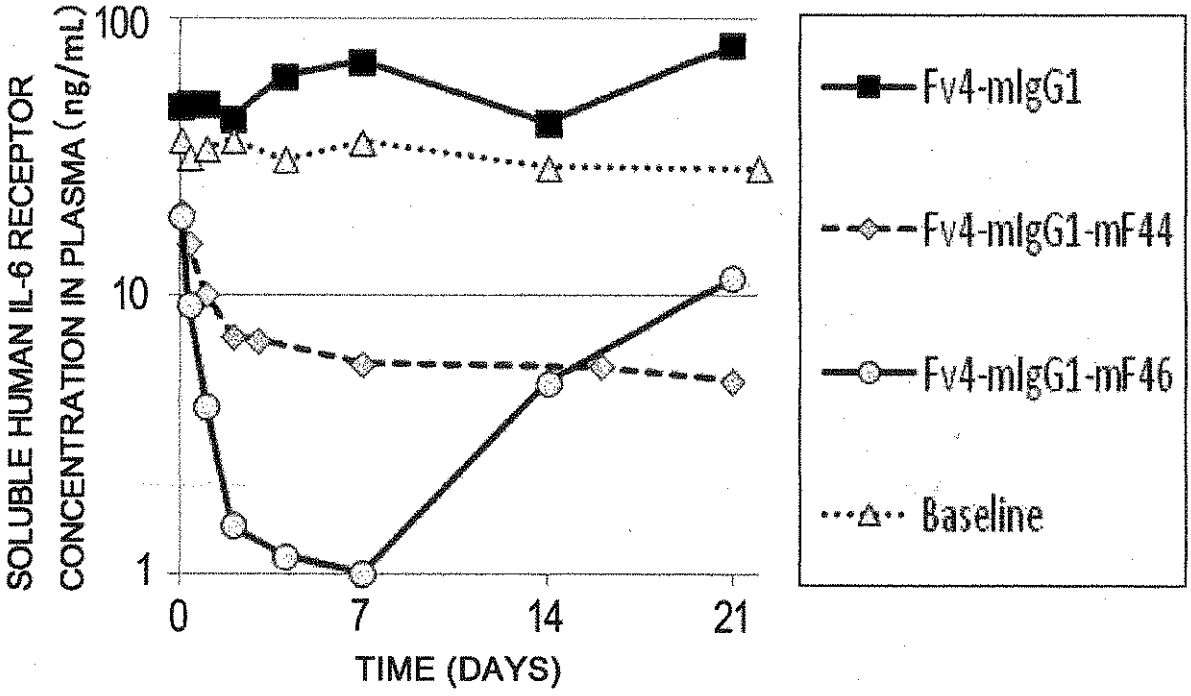

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
Baseline

FIG. 11

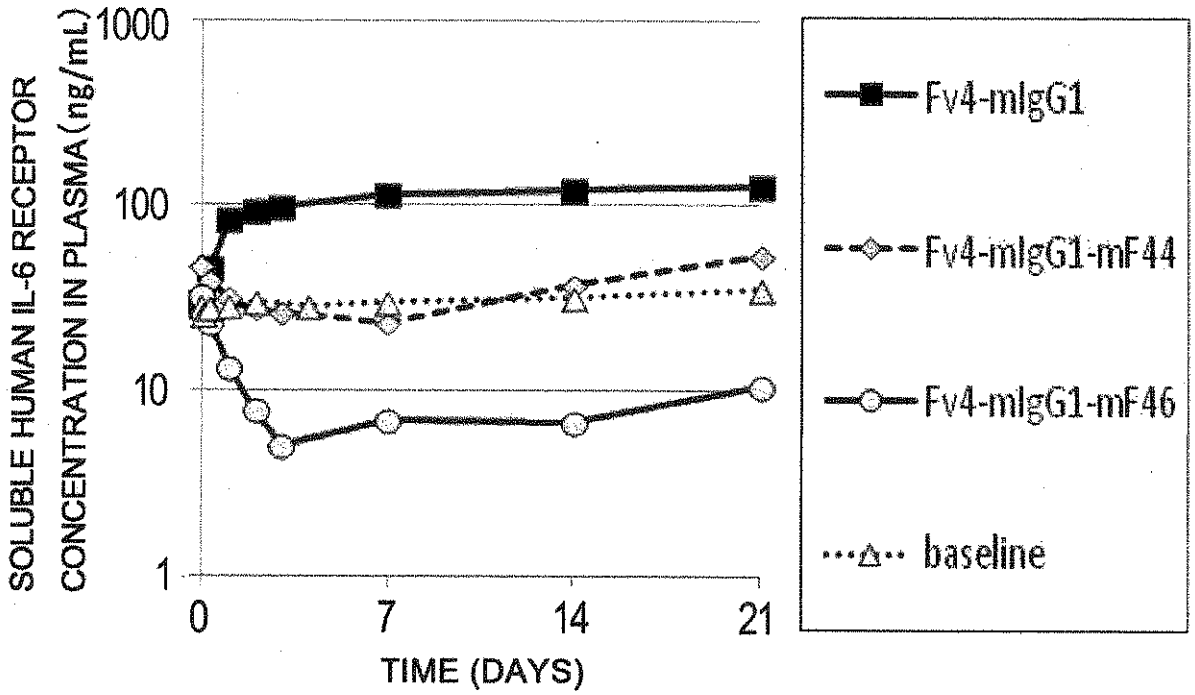

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 12

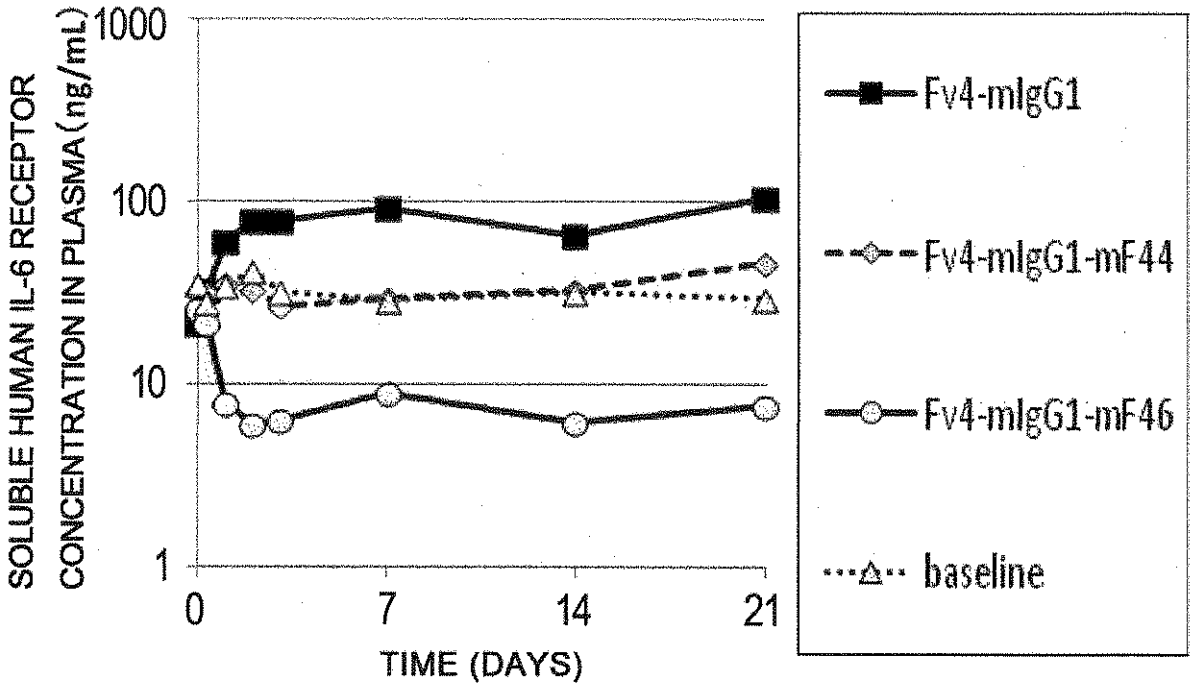

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 13

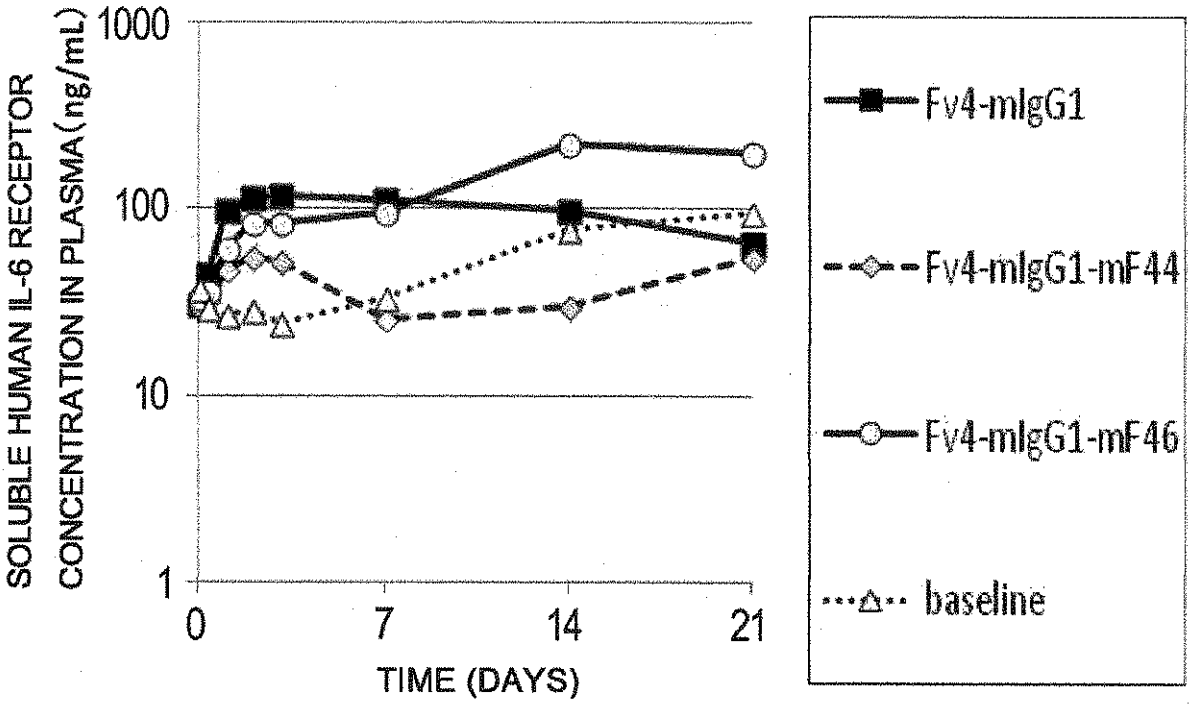

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA(ng/mL)
1000
100
10
1
0
7
14
21
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-mF44
Fv4-mIgG1-mF46
baseline

FIG. 14

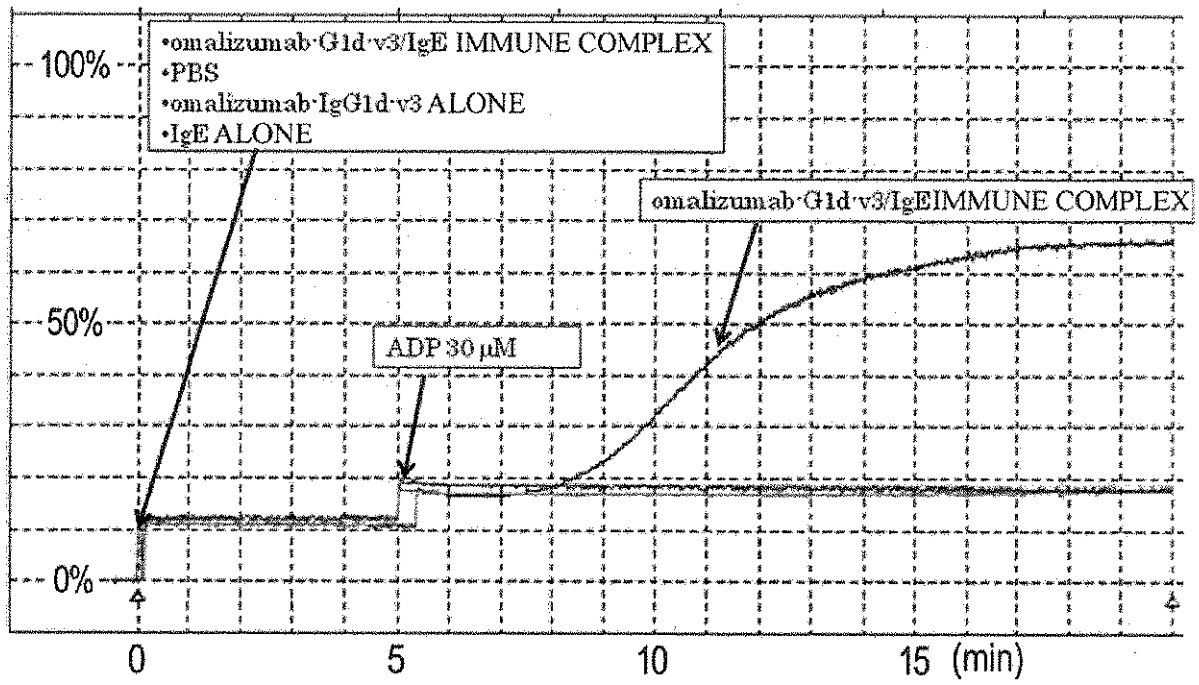

•omalizumab·G1d·v3/IgE IMMUNE COMPLEX
•PBS
•omalizumab·IgG1d·v3 ALONE
•IgE ALONE
omalizumab·G1d·v3/IgEIMMUNE COMPLEX
ADP 30 μM
100%
50%
0%
0
5
10
15 (min)

FIG. 15

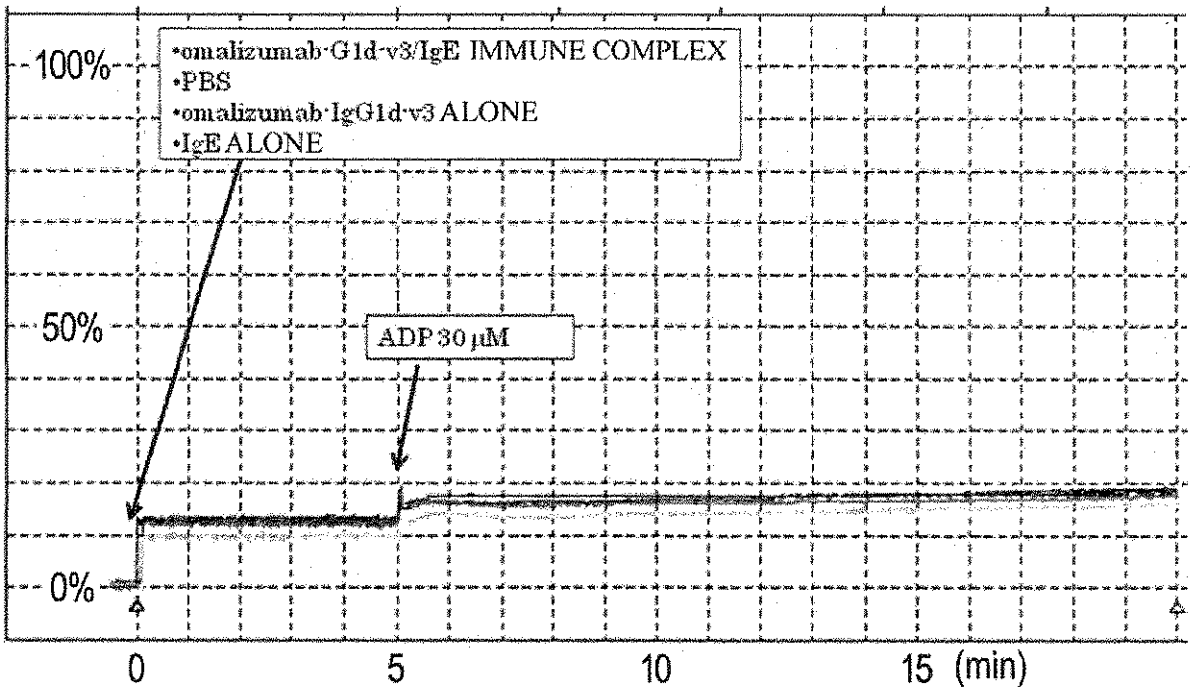

100%
50%
0%
•omalizumab·G1d·v3/IgE IMMUNE COMPLEX
•PBS
•omalizumab·IgG1d·v3 ALONE
•IgE ALONE
ADP 30 μM
0
5
10
15 (min)

FIG. 16

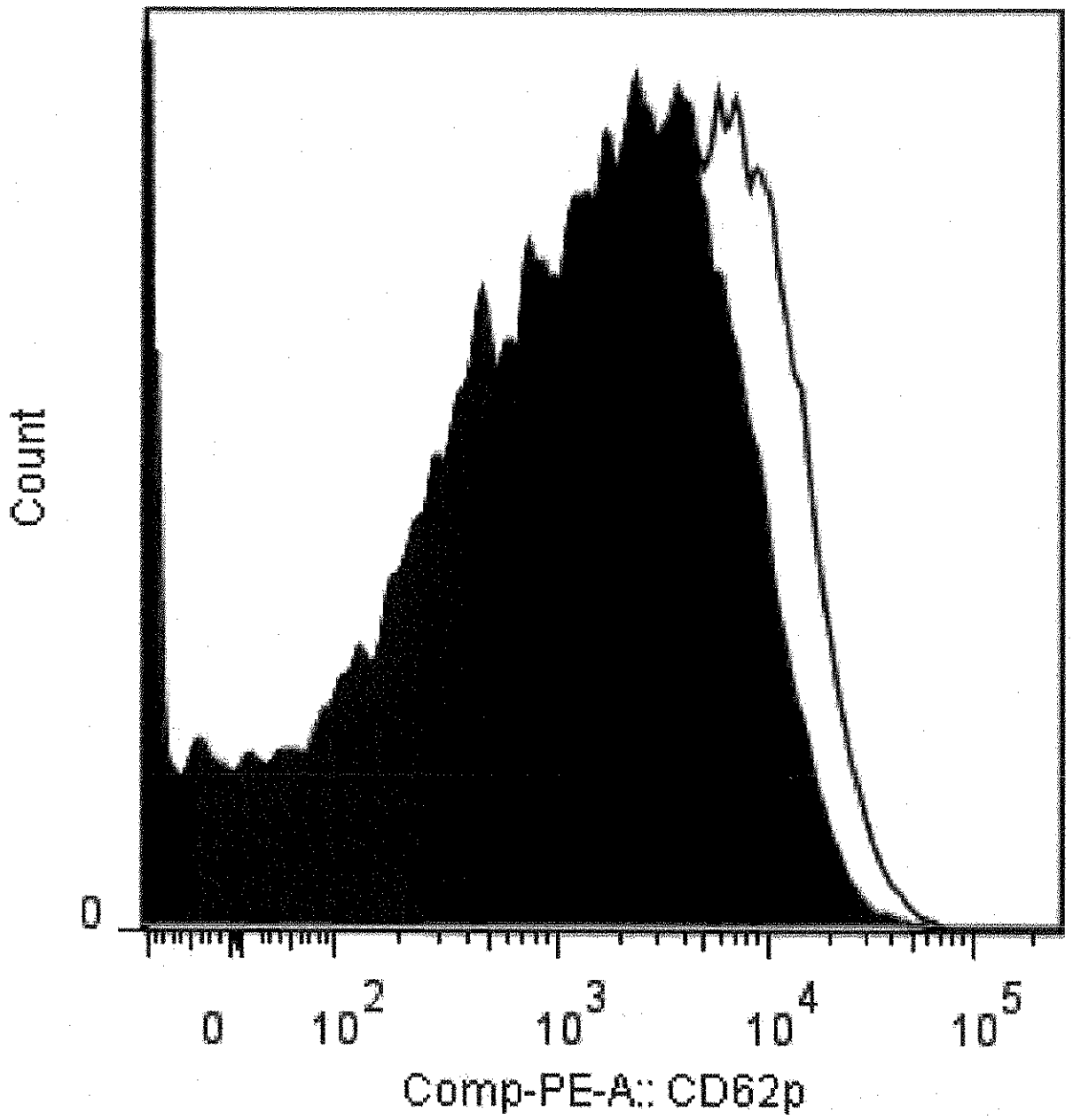


FIG. 17

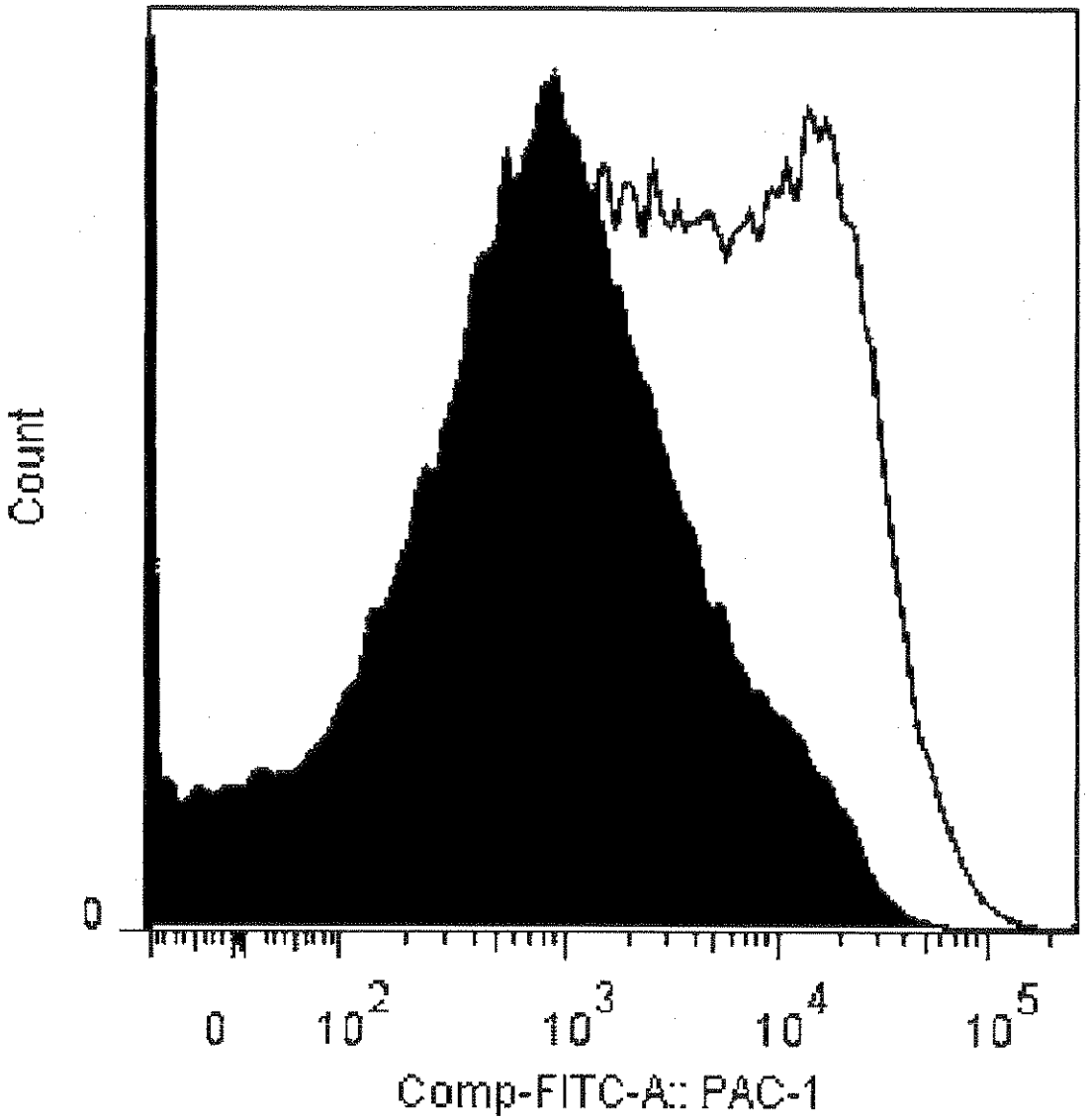


FIG. 18

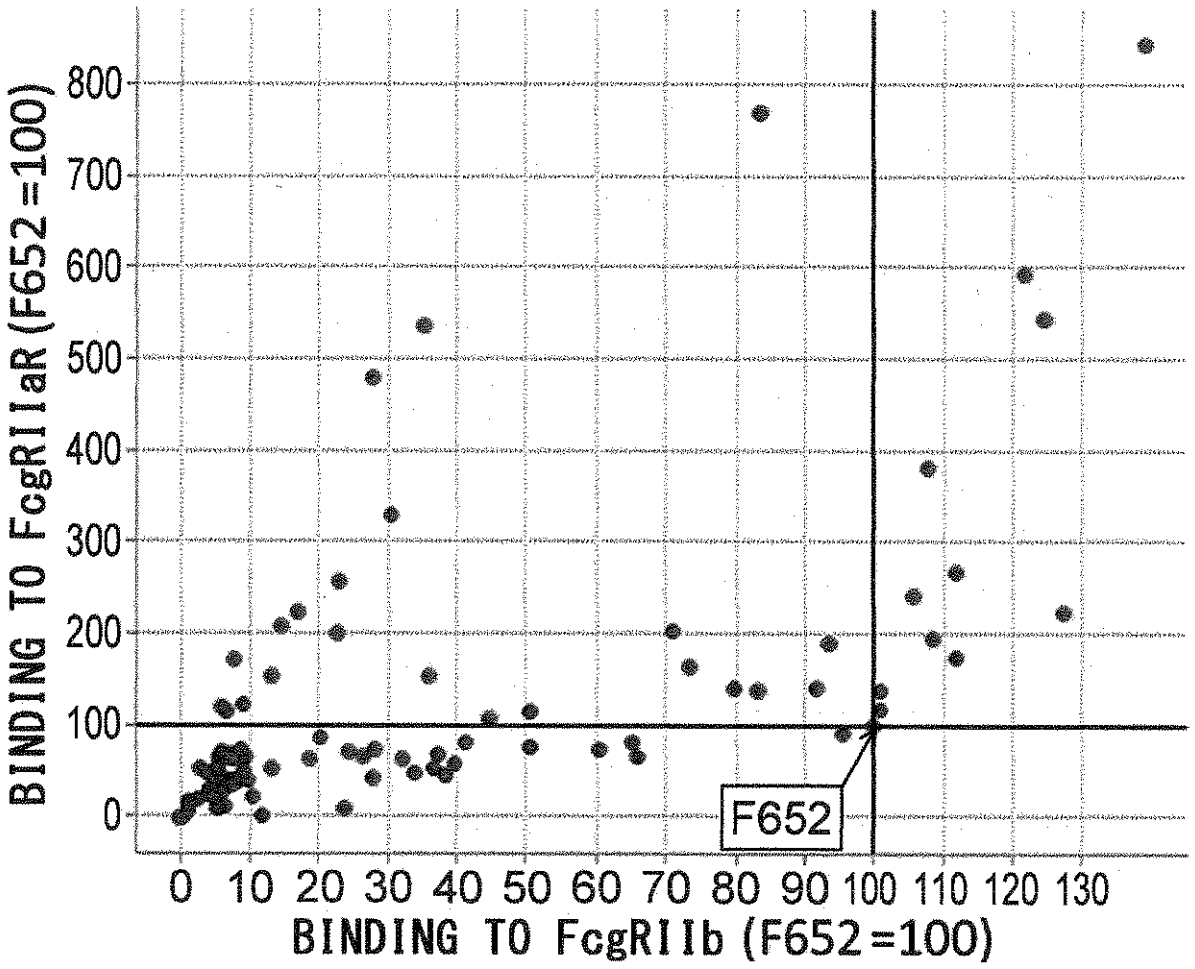

BINDING TO FcgRIIaR (F652=100)
800
700
600
500
400
300
200
100
0
F652
0 10 20 30 40 50 60 70 80 90 100 110 120 130
BINDING TO FcgRIIb (F652=100)

FIG. 19

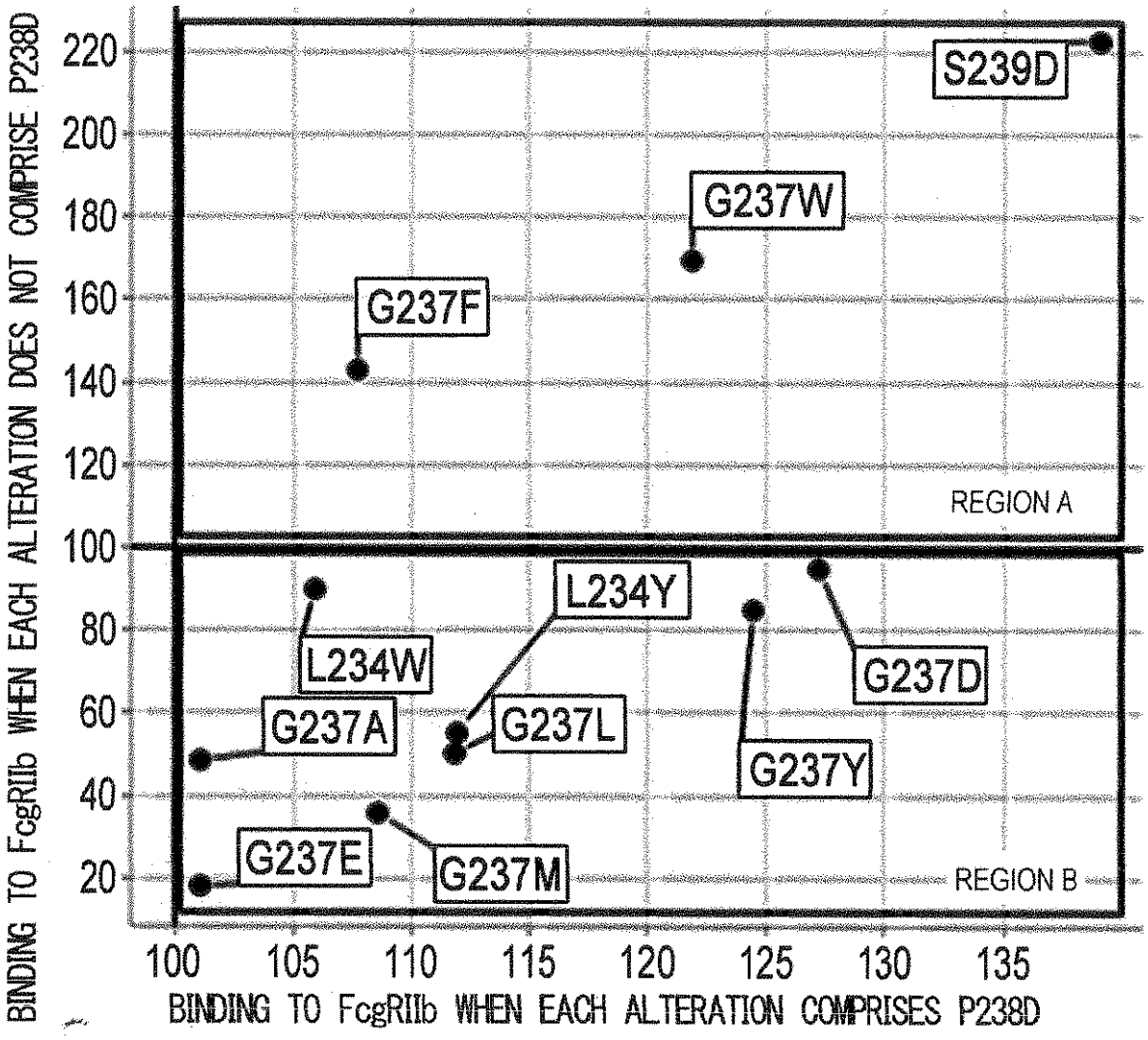

BINDING TO FcgRIIb WHEN EACH ALTERATION DOES NOT COMPRISE P238D
220
200
180
160
140
120
100
80
60
40
20
S239D
G237W
G237F
REGION A
L234Y
L234W
G237D
G237A
G237L
G237Y
G237E
G237M
REGION B
100
105
110
115
120
125
130
135
BINDING TO FcgRIIb WHEN EACH ALTERATION COMPRISES P238D

FIG. 20

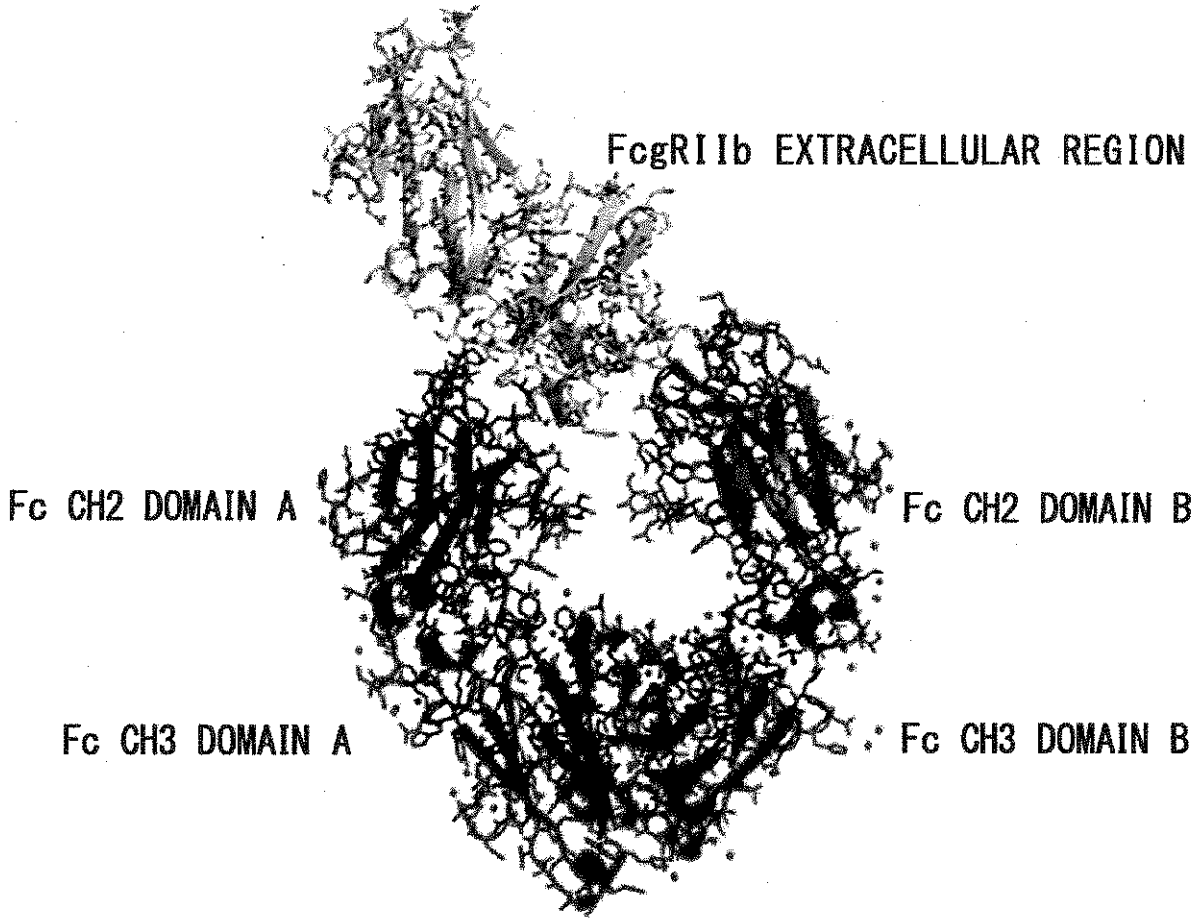
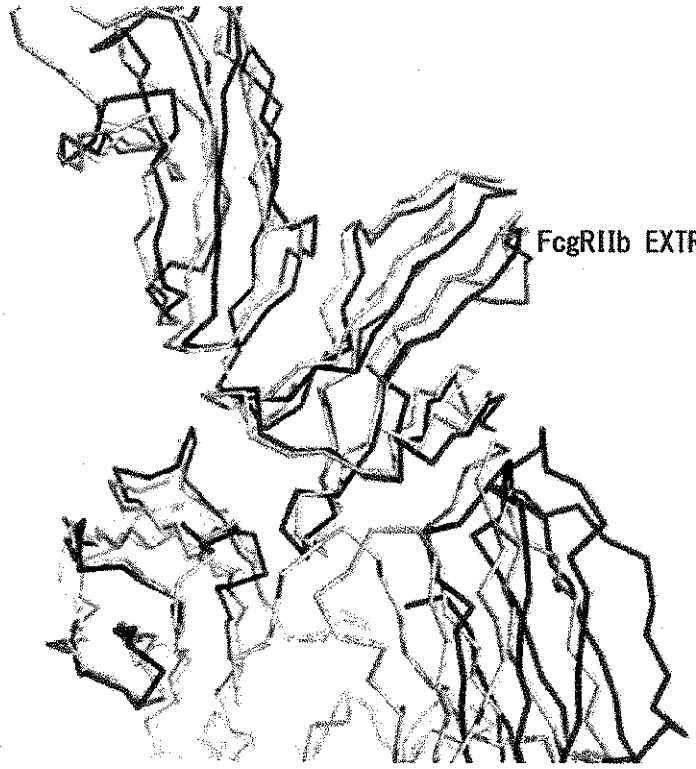
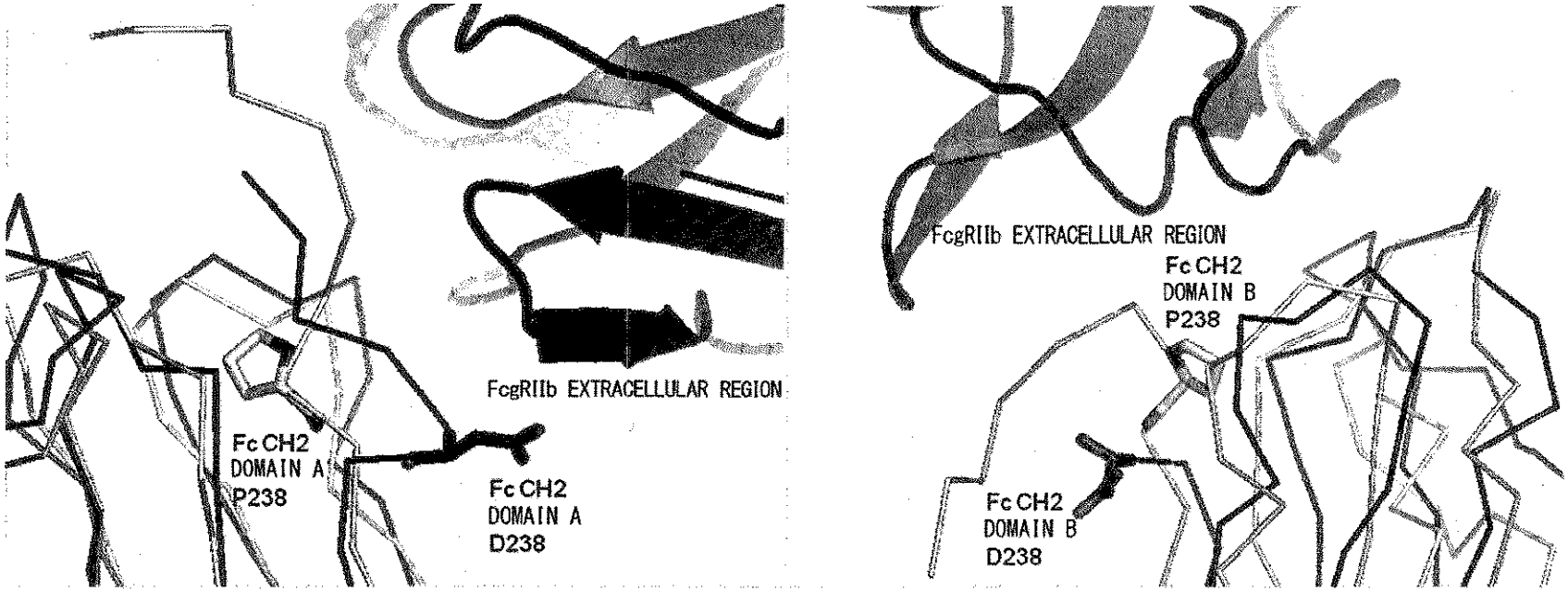

FcgRIIb EXTRACELLULAR REGION
Fc CH2 DOMAIN A
Fc CH2 DOMAIN B
Fc CH3 DOMAIN A
Fc CH3 DOMAIN B

FIG. 21



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/Fcγ RIIb EXTRACELLULAR REGION COMPLEX
GRAY MODEL STRUCTURE OF Fc(WT)/Fcγ RIIb EXTRACELLULAR REGION COMPLEX

FIG. 22



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX

GRAY MODEL STRUCTURE OF Fc(WT)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 23

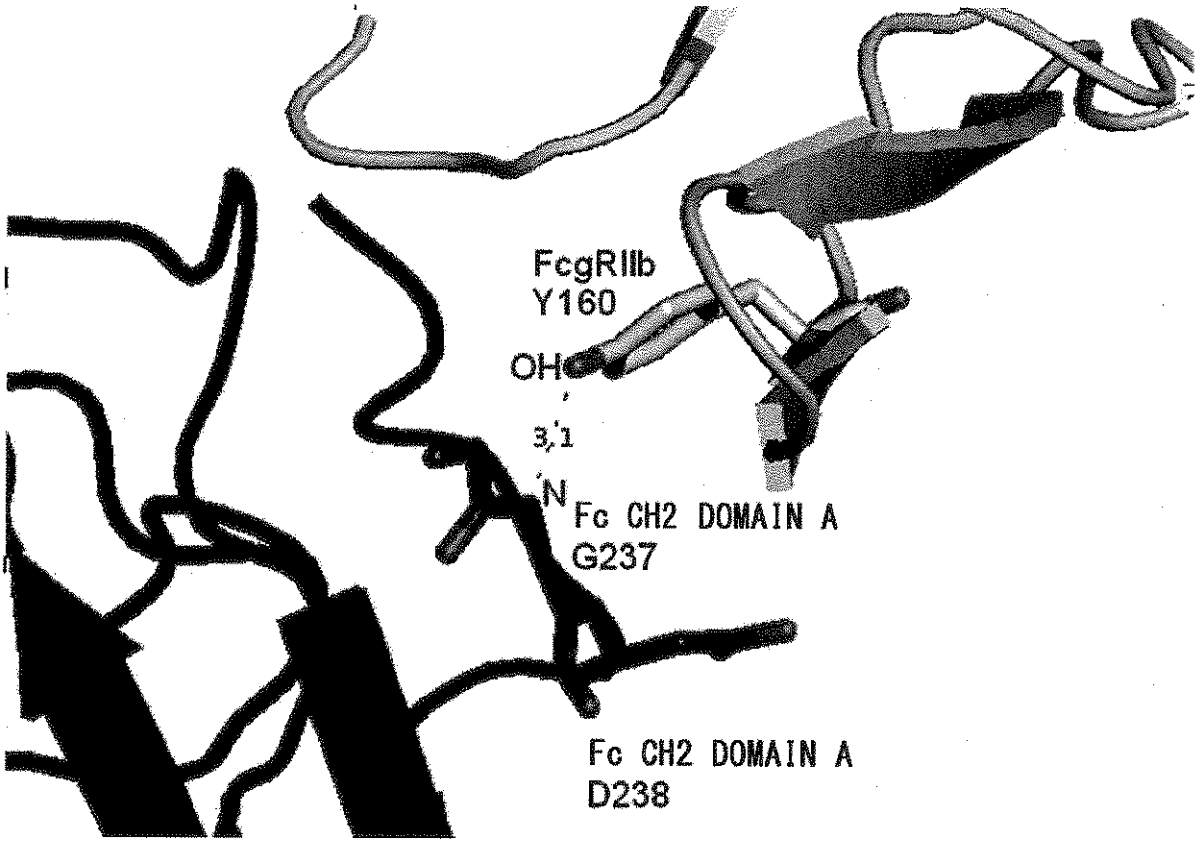


FIG. 24

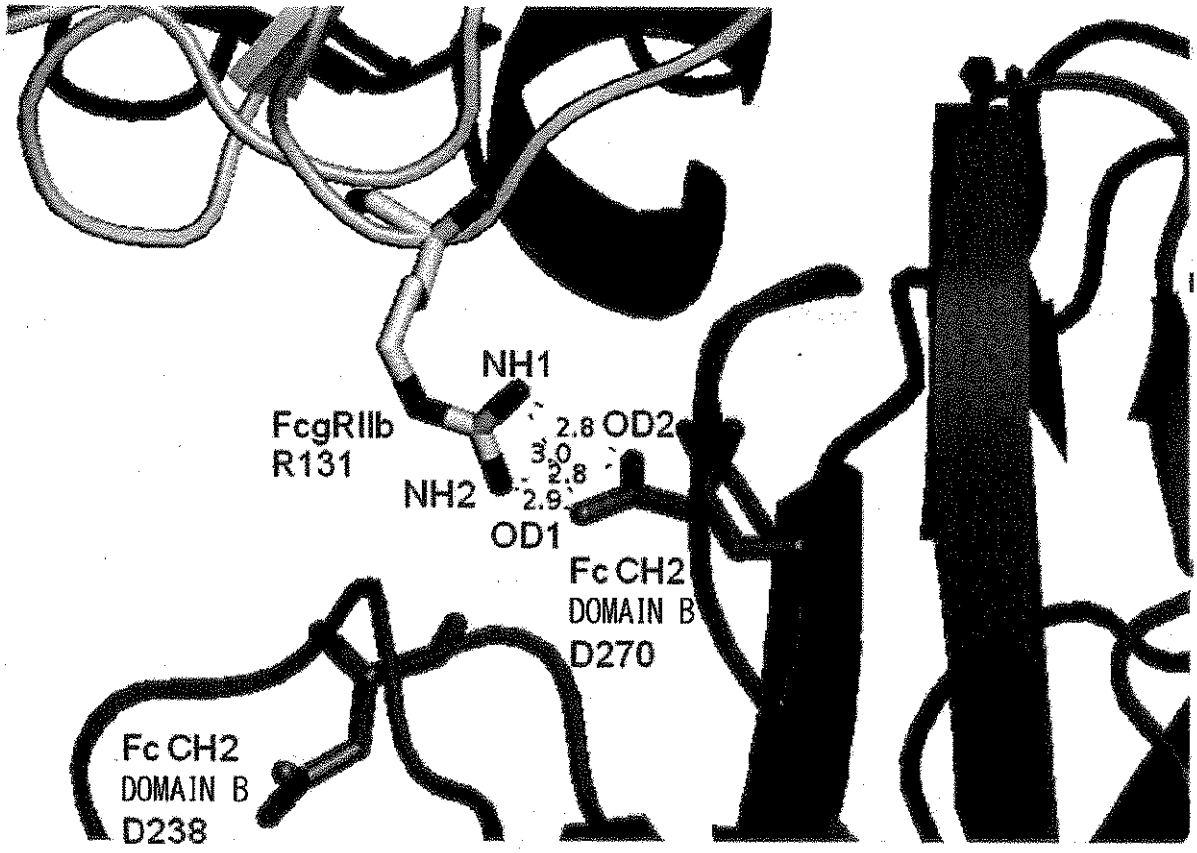

NH1
FcgRIIb
R131
2.8
OD2
3.0
2.8
NH2
2.9
OD1
Fc CH2
DOMAIN B
D270
Fc CH2
DOMAIN B
D238

FIG. 25

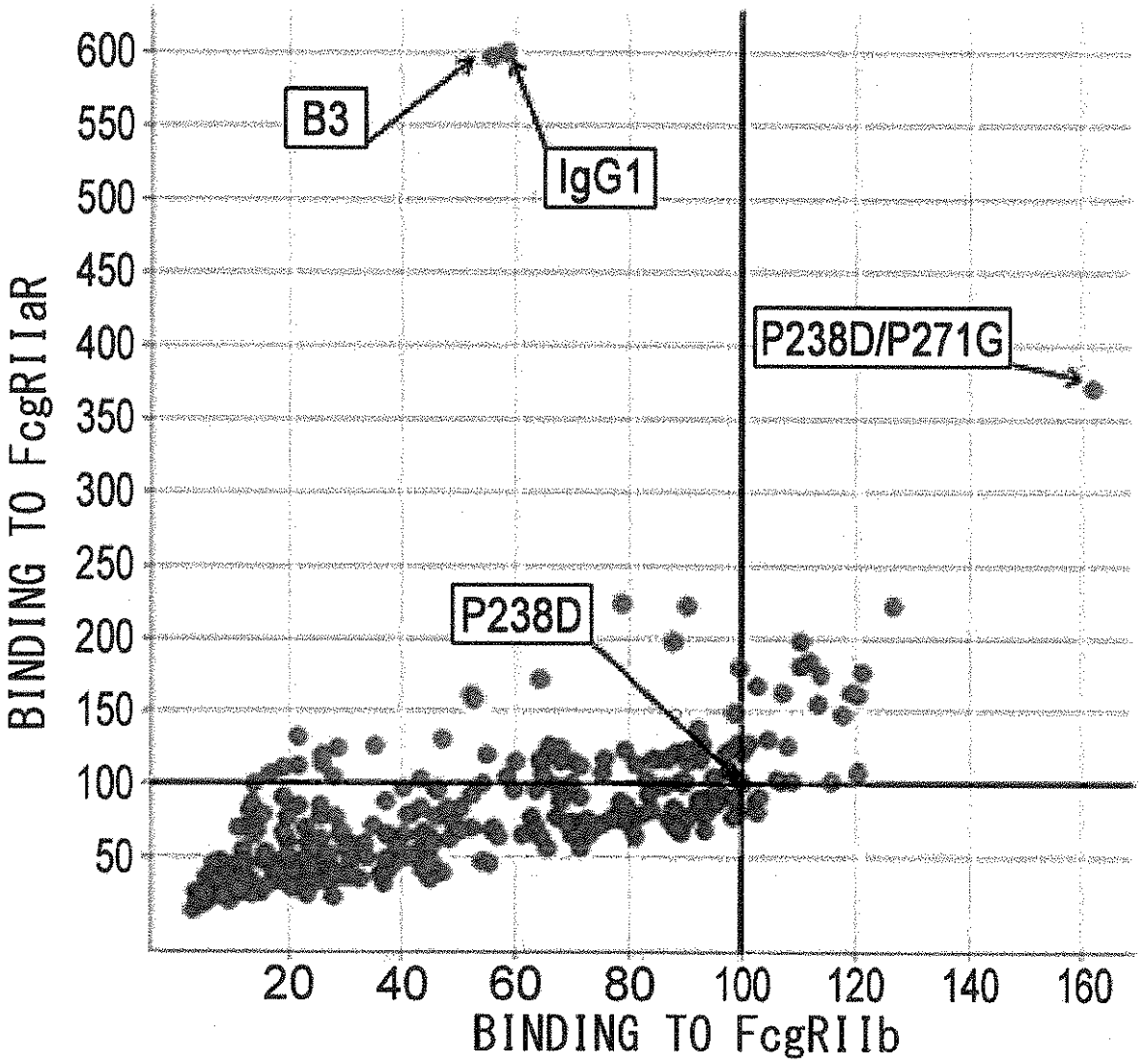

600
550
500
450
400
350
300
250
200
150
100
50
BINDING TO FcgRIIaR
B3
IgG1
P238D/P271G
P238D
20
40
60
80
100
120
140
160
BINDING TO FcgRIIb

FIG. 26

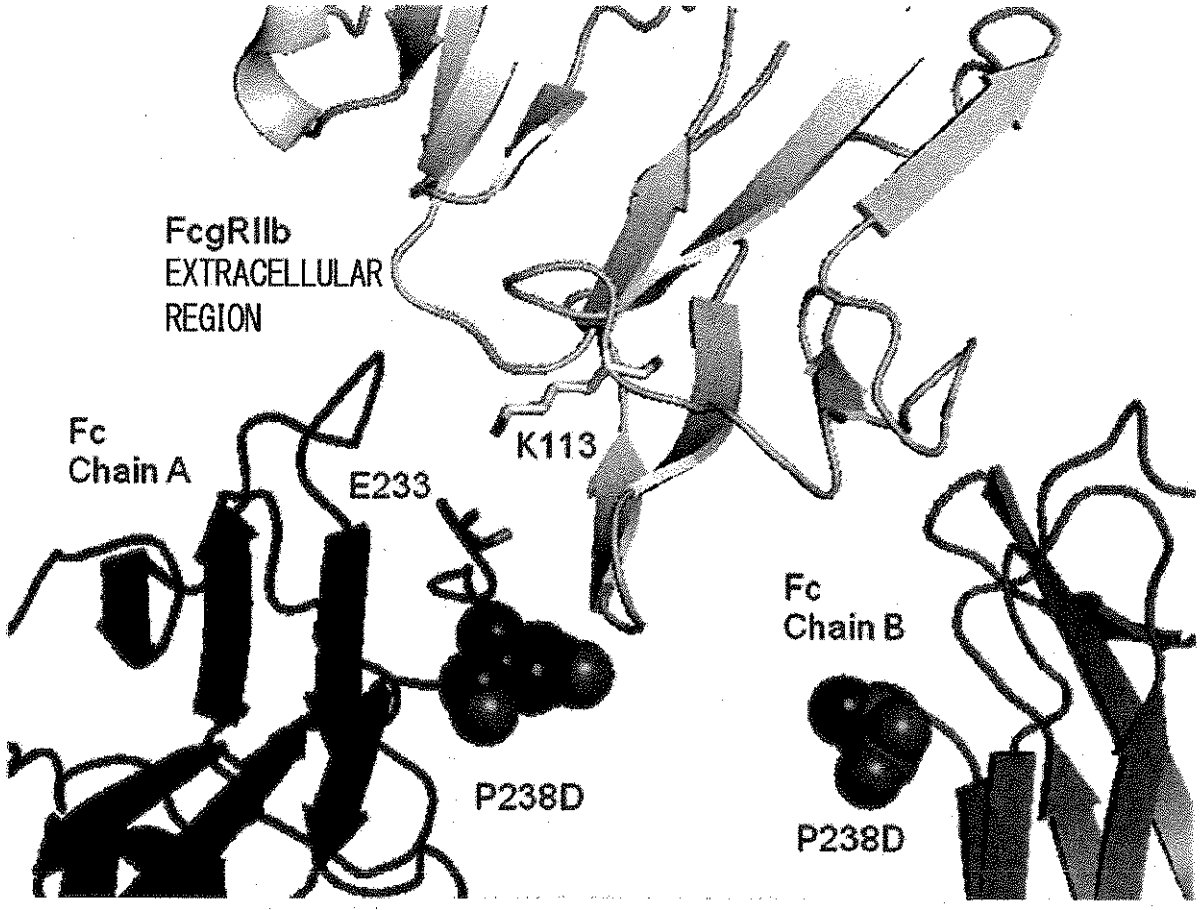

FcgRIIb
EXTRACELLULAR
REGION
Fc
Chain A
E233
K113
P238D
Fc
Chain B
P238D

FIG. 27

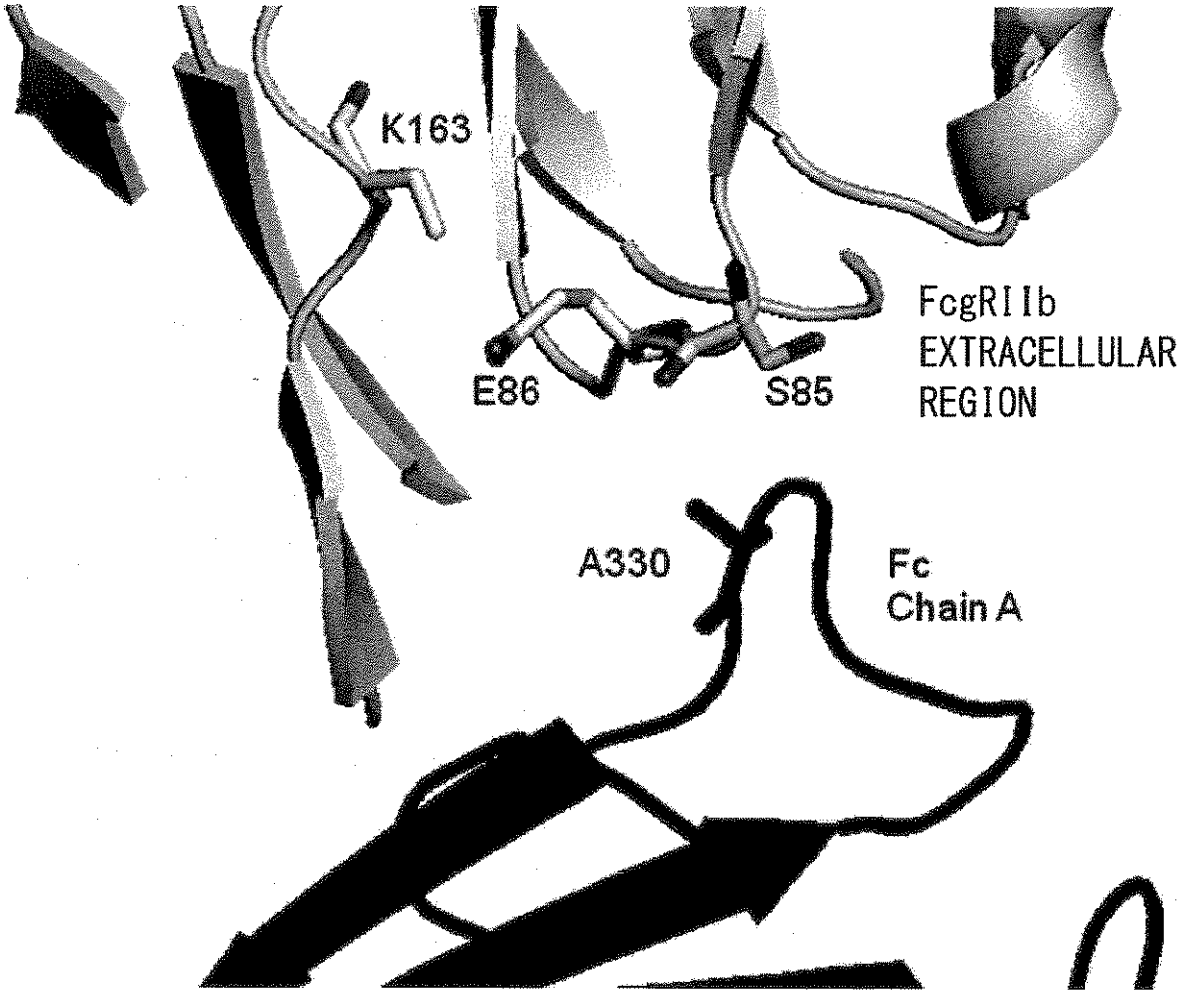
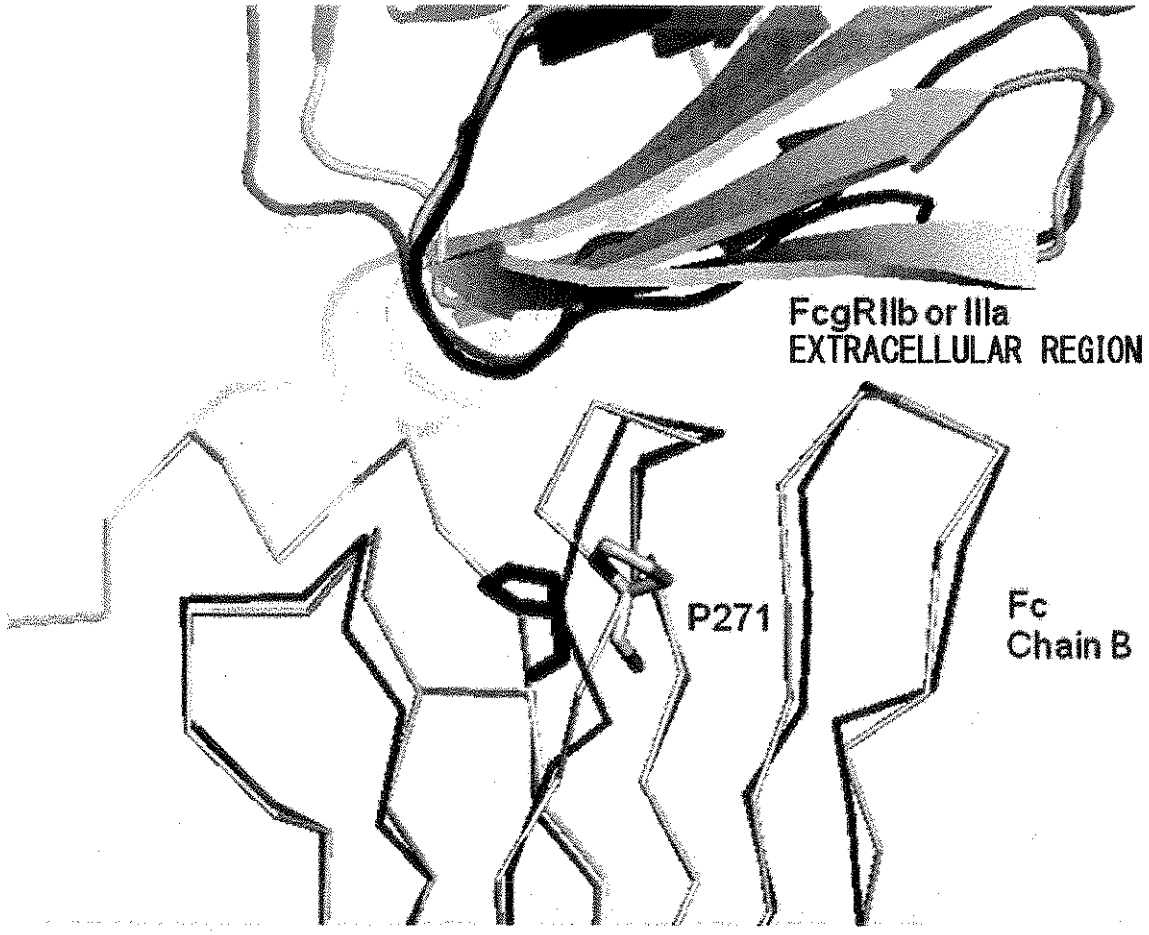


FIG. 28



BLACK CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX
GRAY CRYSTAL STRUCTURE OF Fc(WT)/FcγRIIIa EXTRACELLULAR REGION COMPLEX (PDB code: 3SGJ)

FIG. 29

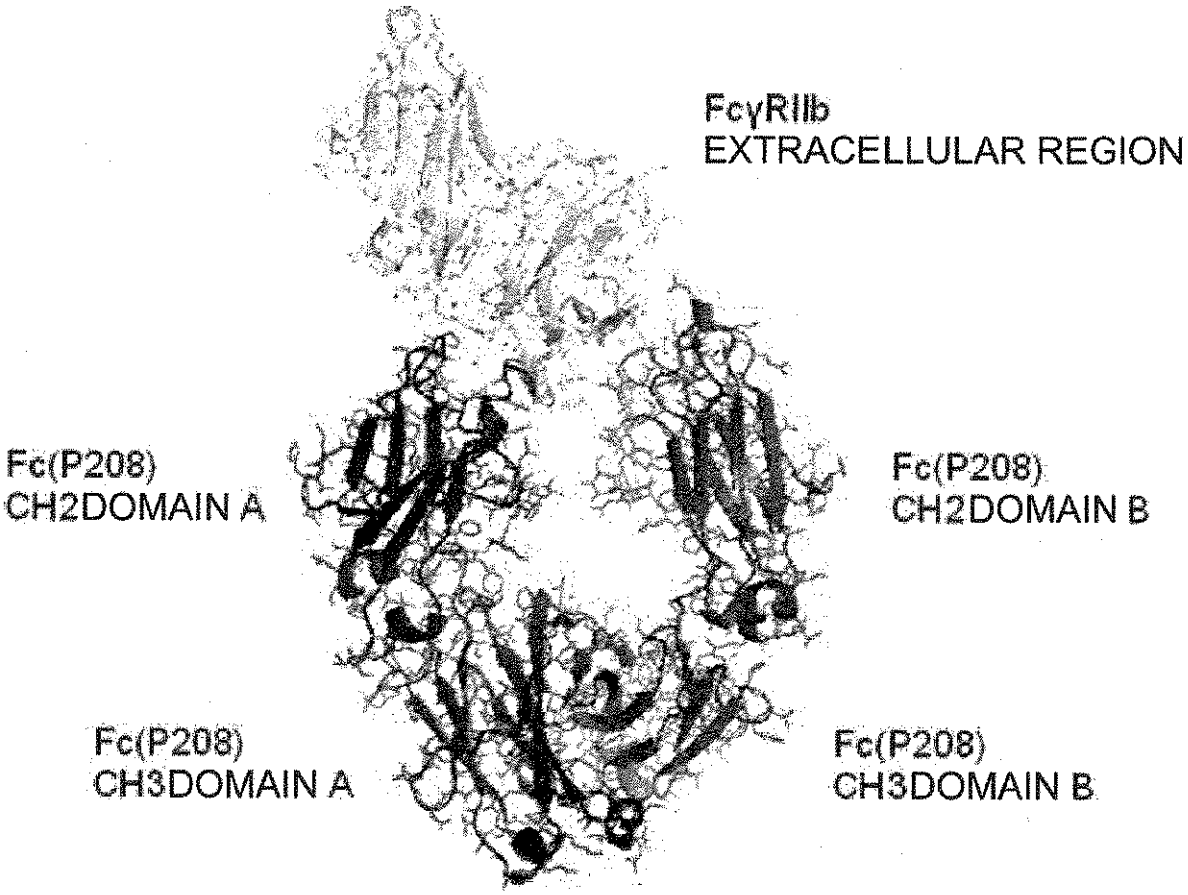
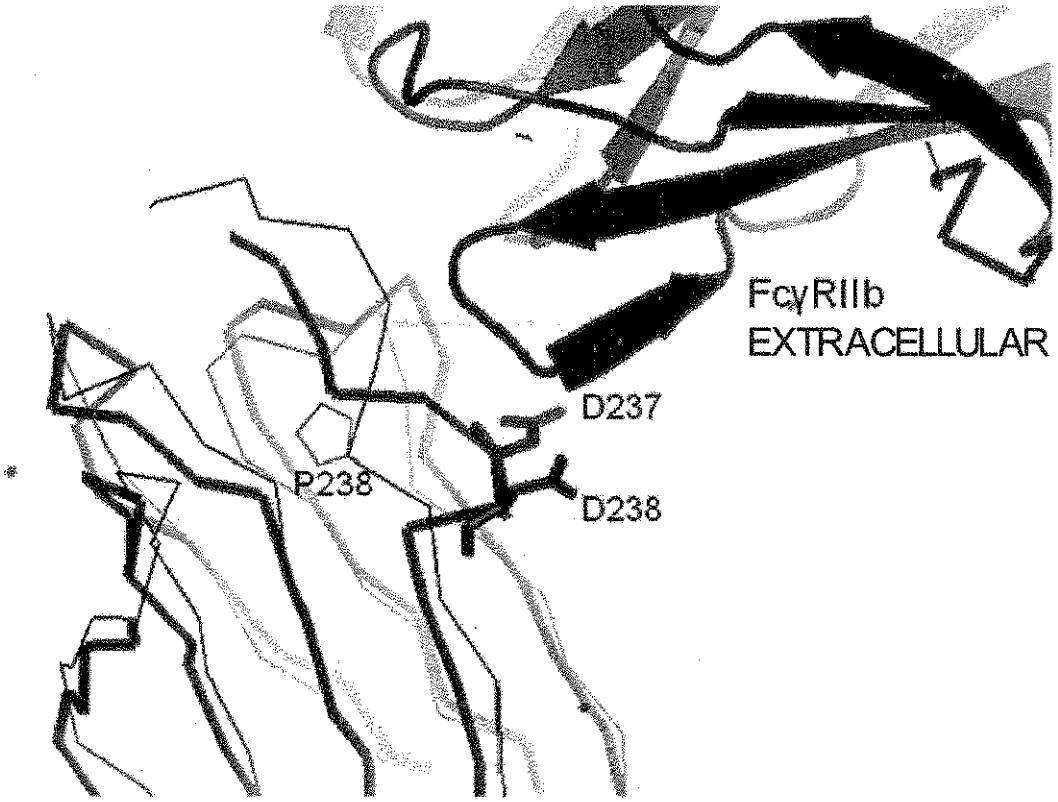

FcγRIIb
EXTRACELLULAR REGION
Fc(P208)
CH2DOMAIN A
Fc(P208)
CH2DOMAIN B
Fc(P208)
CH3DOMAIN A
Fc(P208)
CH3DOMAIN B

FIG. 30



THIN LINE: Fc(Wt) CH2DOMAIN A
HEAVY LINE: Fc(P208) CH2DOMAIN A

FIG. 31

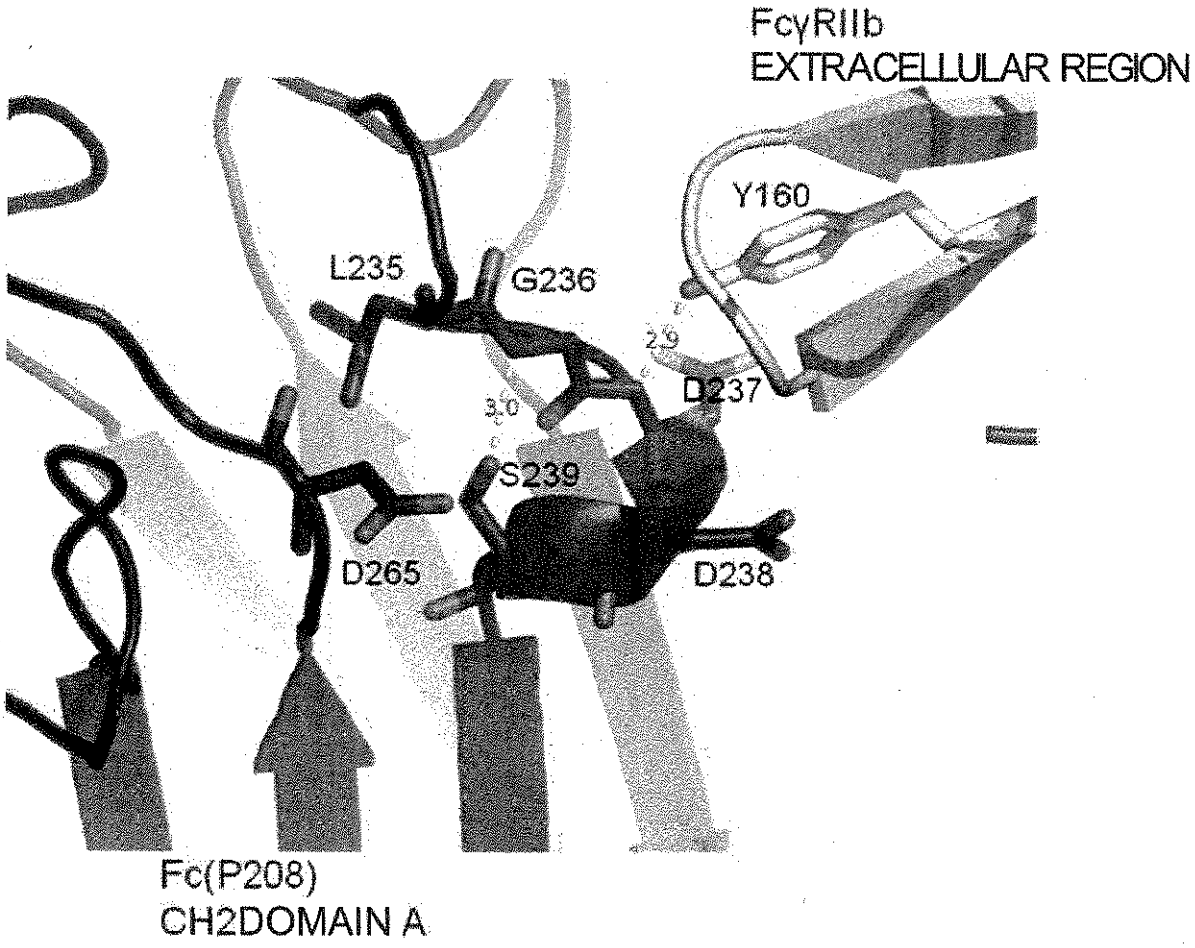

FcγRIIb
EXTRACELLULAR REGION
Y160
L235
G236
2.9
D237
3.0
S239
D265
D238
Fc(P208)
CH2DOMAIN A

FIG. 32

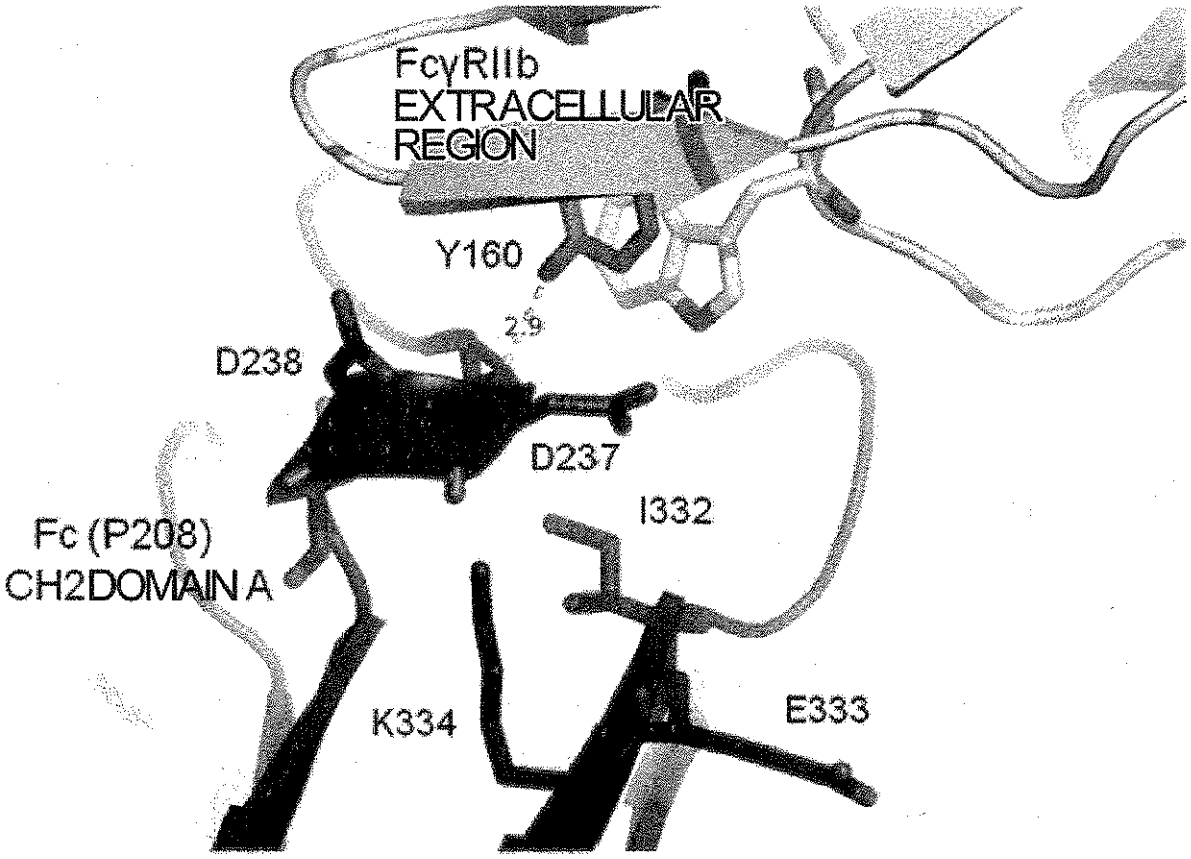
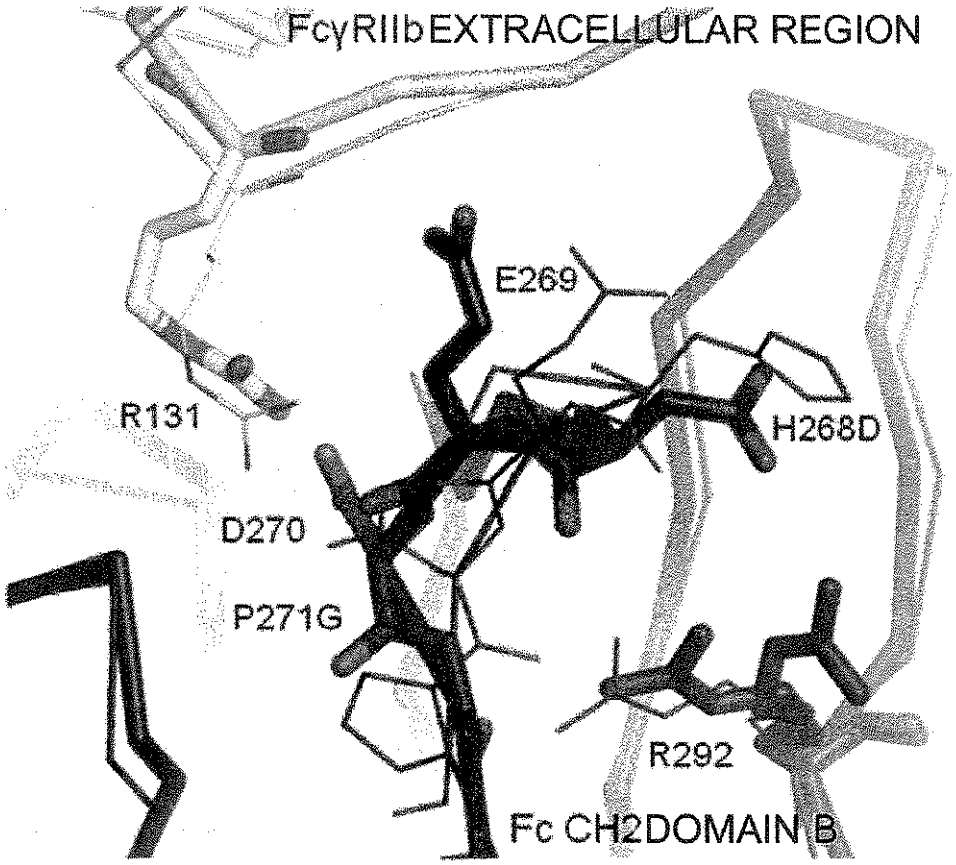
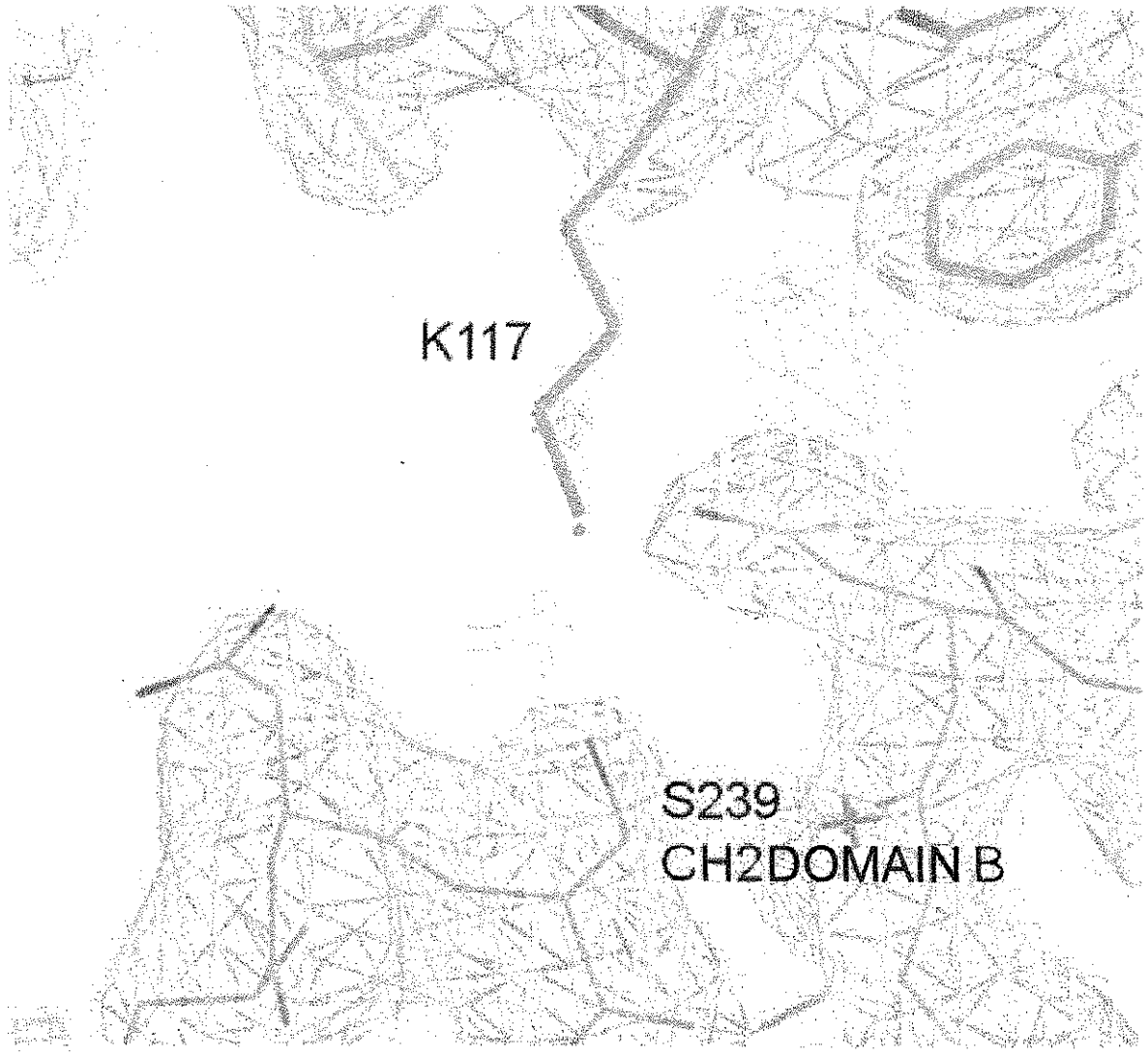

FcγRIIb
EXTRACELLULAR
REGION
Y160
2.9
D238
D237
I332
Fc (P208)
CH2DOMAIN A
K334
E333

FIG. 33



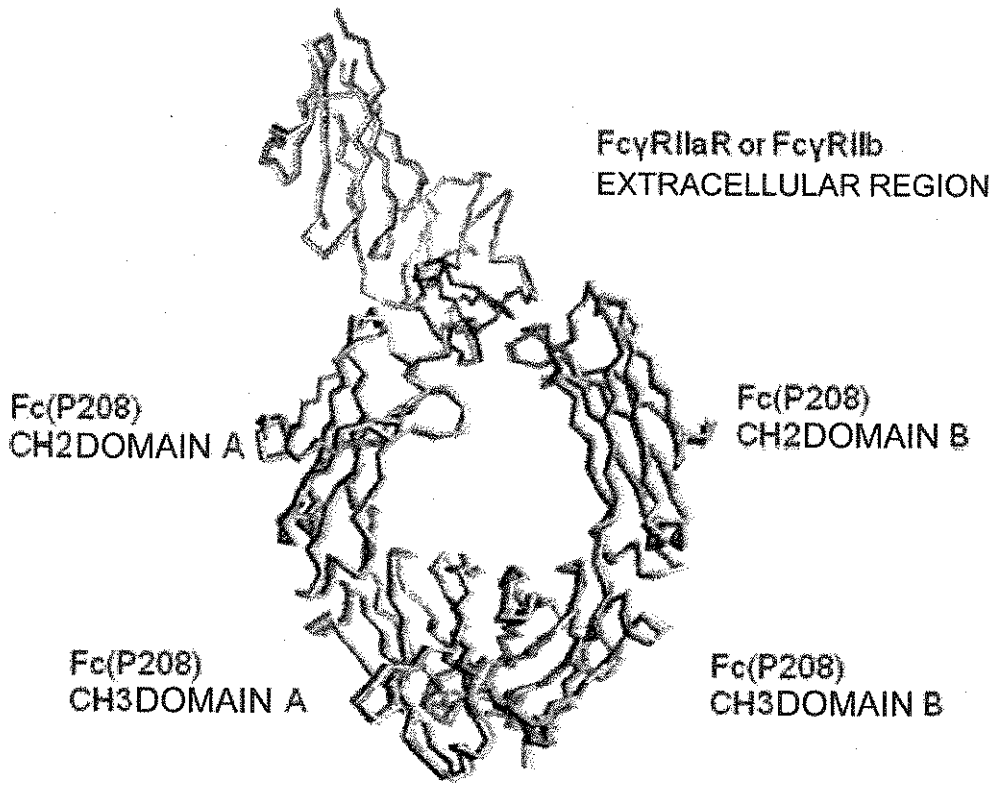
THIN LINE: X-RAY CRYSTAL STRUCTURE OF Fc(P238D)/FcγRIIb EXTRACELLULAR REGION COMPLEX
HEAVY LINE: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 34



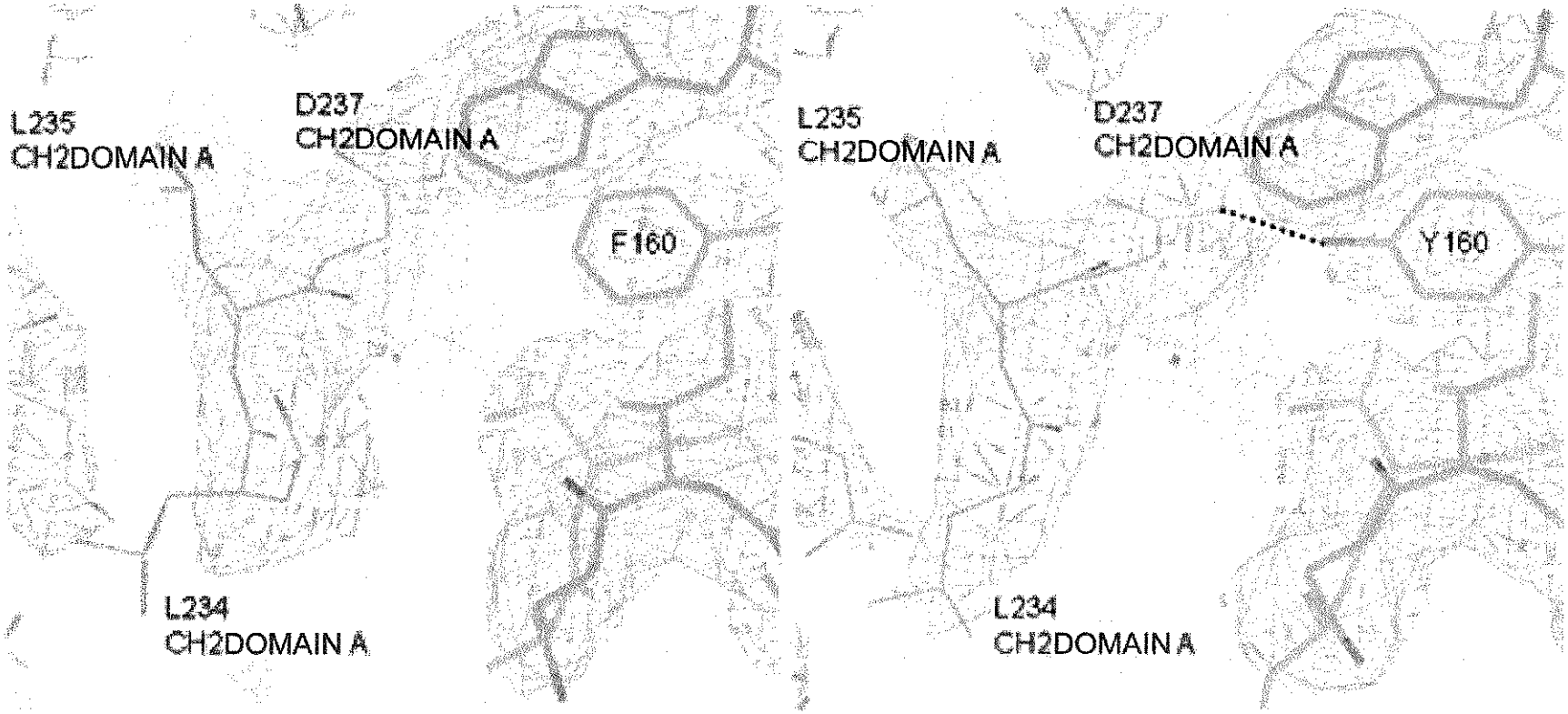
THIN LINE : Fc(P208)
HEAVY LINE : FcγRIIb EXTRACELLULAR REGION

FIG. 35



BLACK: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX
GRAY: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 36



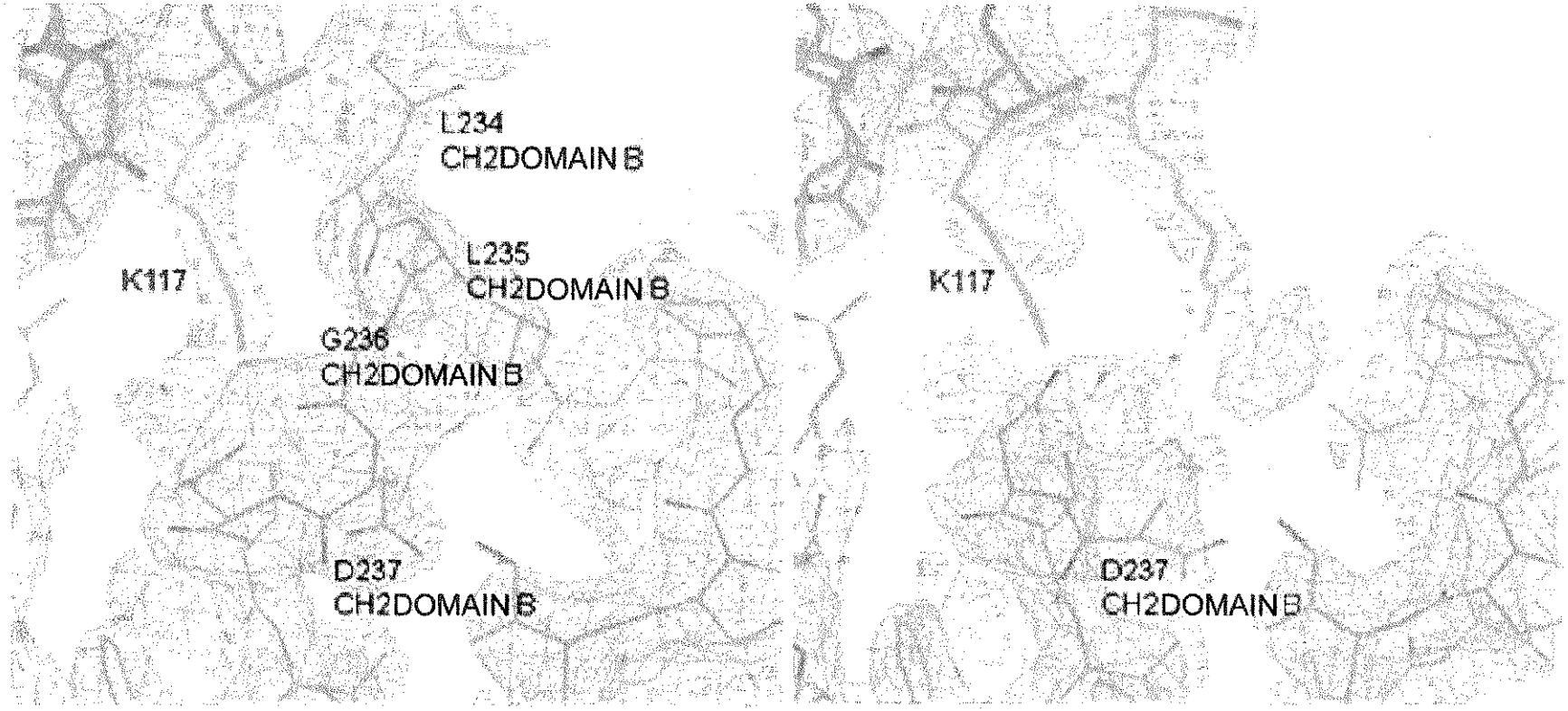
THIN LINE: Fc(P208)

HEAVY LINE: FcγRIIaR or FcγRIIb EXTRACELLULAR REGION

LEFT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX

RIGHT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 37



THIN LINE: Fc(P208)

HEAVY LINE: FcγRIIaR or FcγRIIb EXTRACELLULAR REGION

LEFT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIaR EXTRACELLULAR REGION COMPLEX

RIGHT: X-RAY CRYSTAL STRUCTURE OF Fc(P208)/FcγRIIb EXTRACELLULAR REGION COMPLEX

FIG. 38

```
G1d  118 ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
G4d  118 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPS

G1d  208 NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
G4d  208 NTKVDKRVESK---YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN

G1d  298 STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
G4d  298 STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP

G1d  388 ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 80)
G4d  388 ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSL (SEQ ID NO: 81)
```

FIG. 39

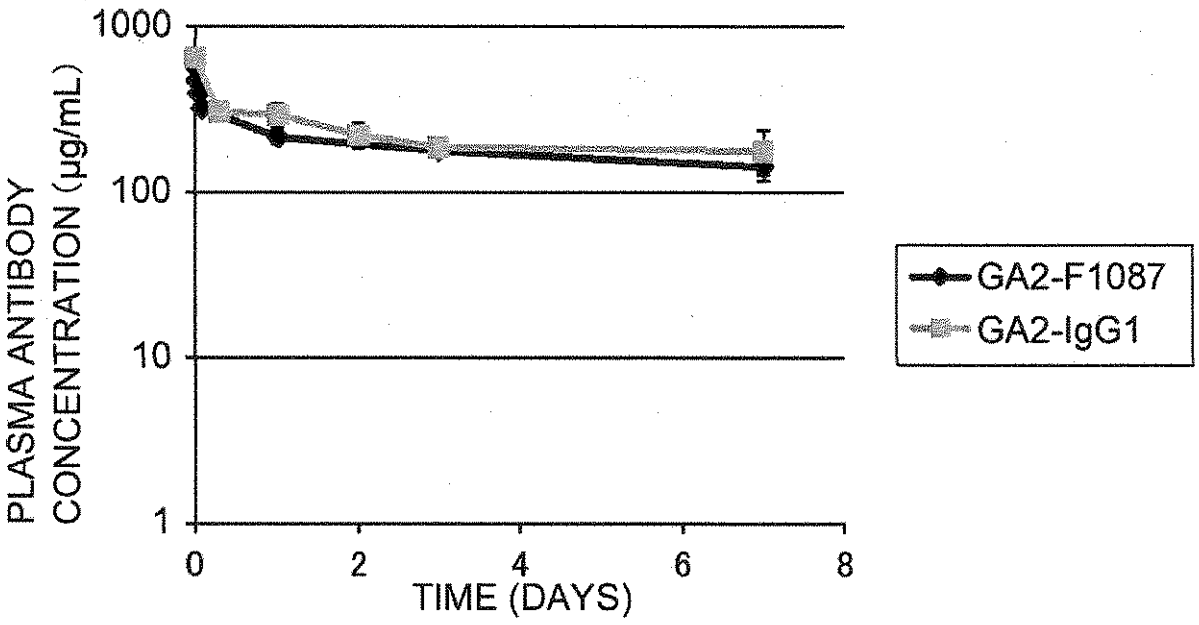

1000
100
10
1
PLASMA ANTIBODY CONCENTRATION (µg/mL)
0
2
4
6
8
TIME (DAYS)
GA2-F1087
GA2-IgG1

FIG. 40

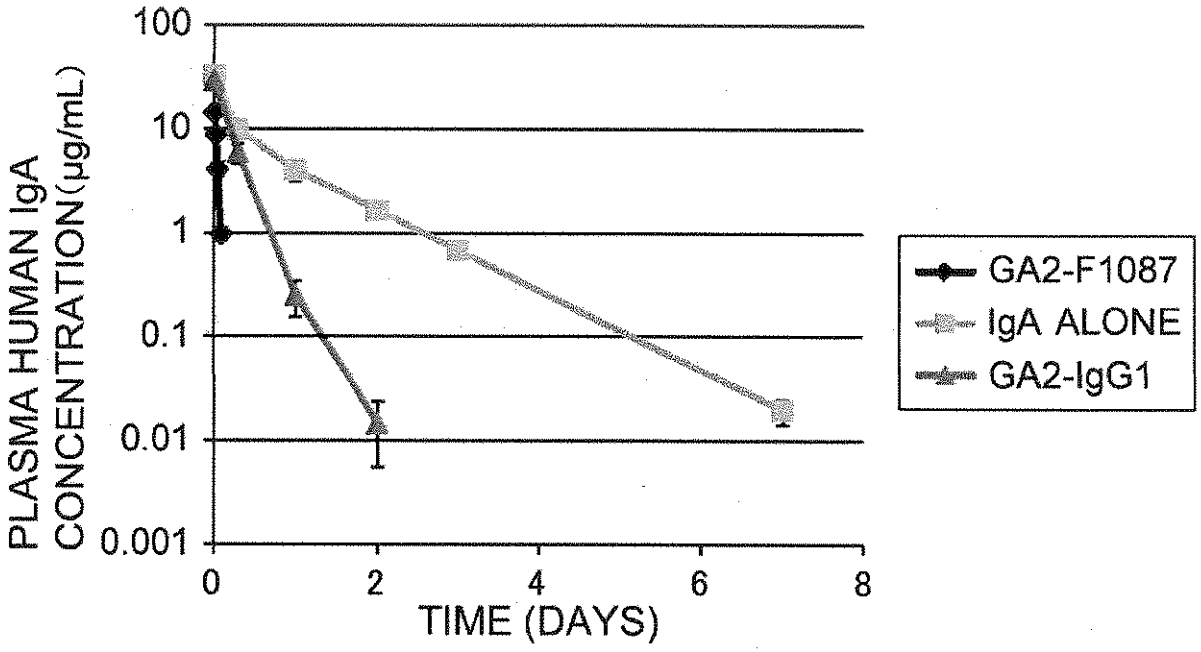

100
10
1
0.1
0.01
0.001
PLASMA HUMAN IgA CONCENTRATION(μg/mL)
0
2
4
6
8
TIME (DAYS)
GA2-F1087
IgA ALONE
GA2-IgG1

FIG. 41

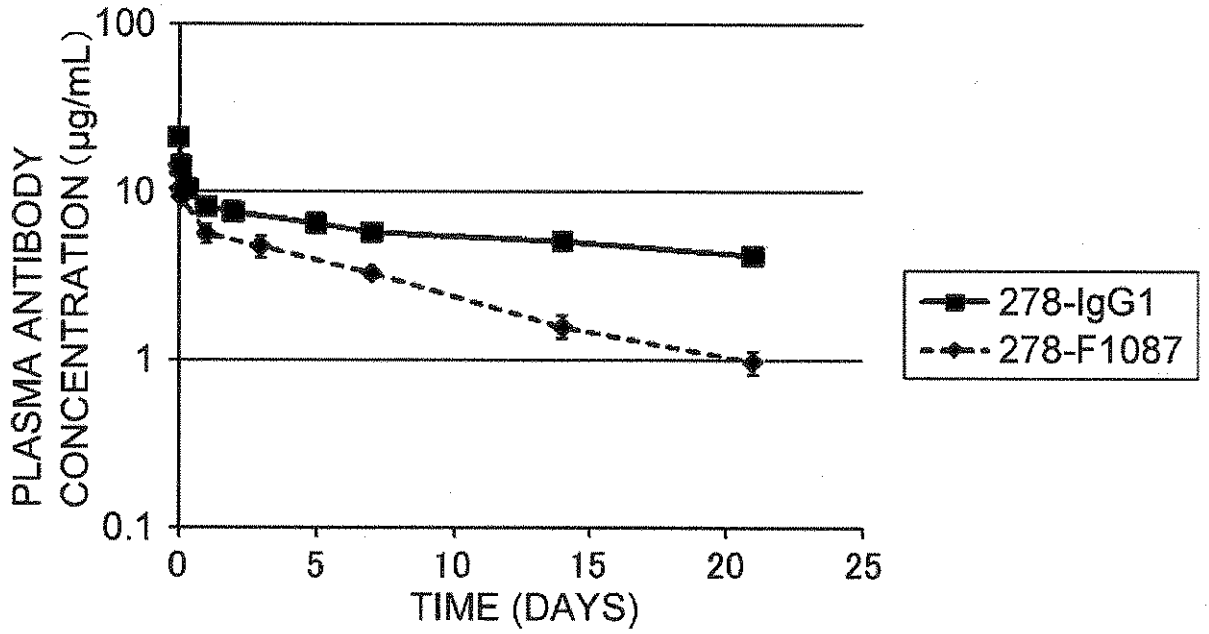

PLASMA ANTIBODY CONCENTRATION (μg/mL)
100
10
1
0.1
0
5
10
15
20
25
TIME (DAYS)
278-IgG1
278-F1087

FIG. 42

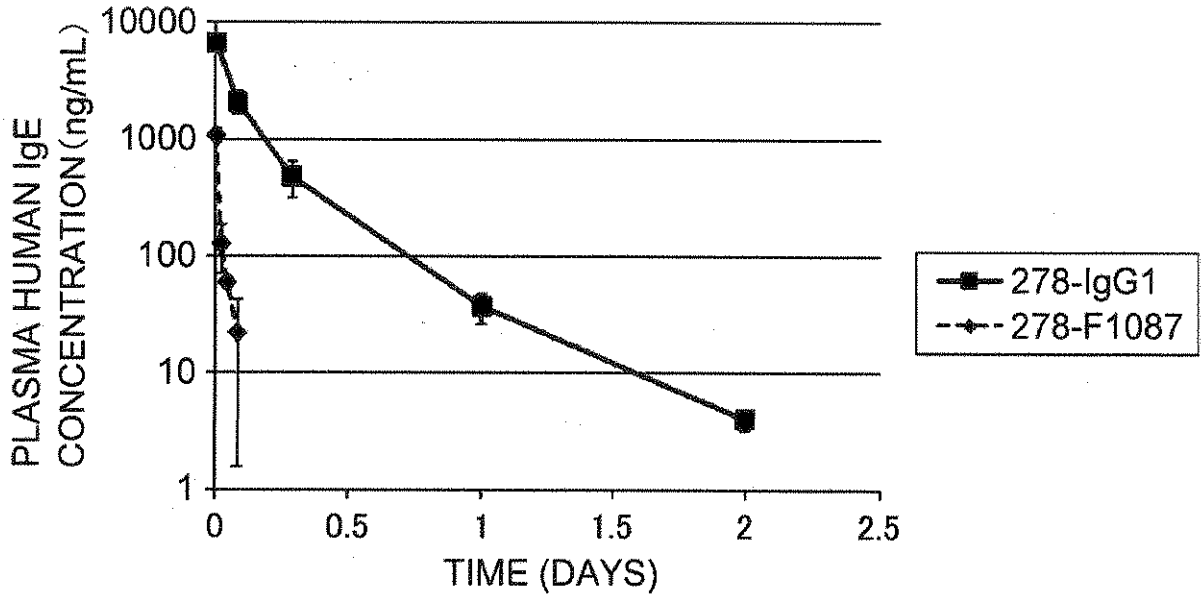

PLASMA HUMAN IgE CONCENTRATION (ng/mL)
10000
1000
100
10
1
0
0.5
1
1.5
2
2.5
TIME (DAYS)
278-IgG1
278-F1087

FIG. 43

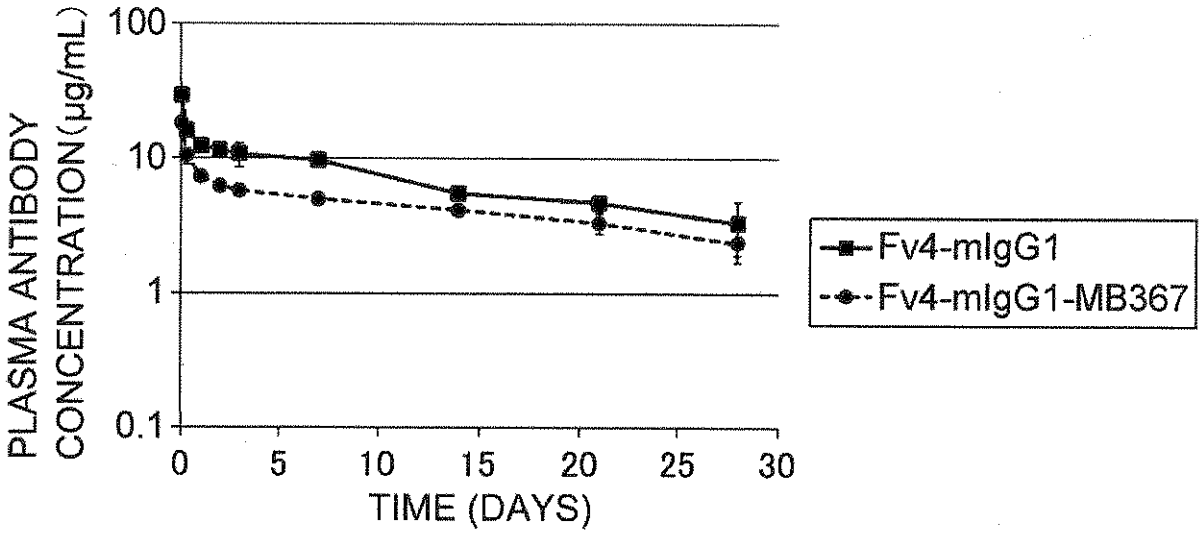

PLASMA ANTIBODY CONCENTRATION (μg/mL)
100
10
1
0.1
0
5
10
15
20
25
30
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-MB367

FIG. 44

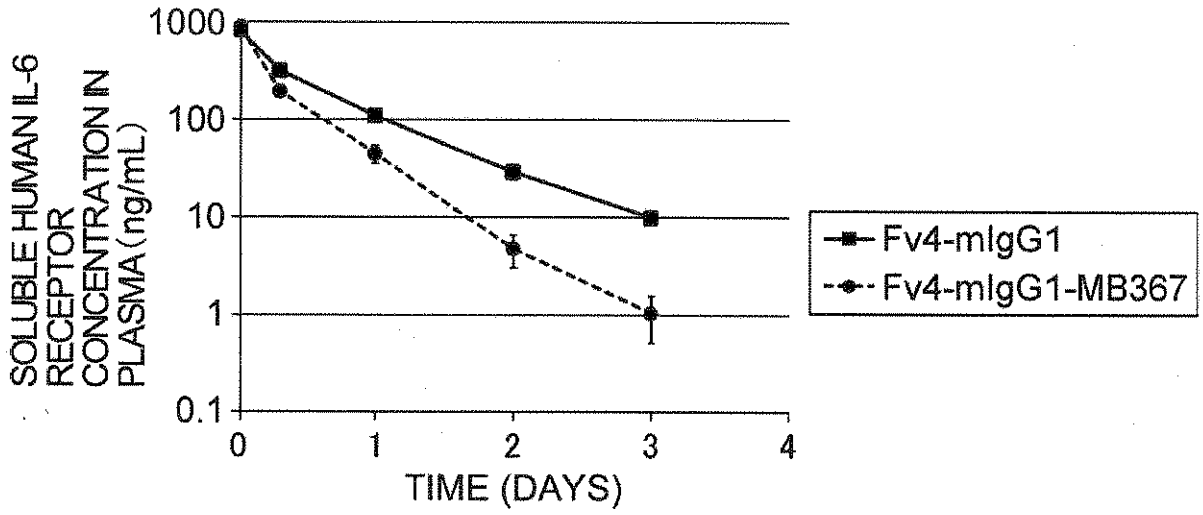

SOLUBLE HUMAN IL-6 RECEPTOR CONCENTRATION IN PLASMA (ng/mL)
1000
100
10
1
0.1
0
1
2
3
4
TIME (DAYS)
Fv4-mIgG1
Fv4-mIgG1-MB367

FIG. 45